SERUM PROCALCITONIN AS A DIAGNOSTIC MARKER OF BACTERIAL INFECTION IN FEBRILE CHILDREN

Submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

in partial fulfillment of regulations

for award of the degree of

M.D (PAEDIATRICS)
BRANCH – VII

ESIC MEDICAL COLLEGE & PGIMSR
K.K.NAGAR ,CHENNAI

THE TAMILNADU DR. M.G.R MEDICAL UNIVERSITY
CHENNAI, TAMILNADU

APRIL 2015

BONAFIDE CERTIFICATE

This is to certify that the dissertation named **"Serum procalcitonin as a diagnostic marker of bacterial infection in febrile children"** is a bonafide work performed by Dr. K. Brindha, post graduate student, Department of Paediatrics, ESIC Medical College & PGIMSR, Chennai-78, under my guidance and supervision in fulfillment of regulations of The Tamilnadu Dr. M.G.R Medical University for the award of M.D. Degree during the academic year 2012-2015

GUIDE:

Prof. Dr. Sowmya Sampath
M.D., D.N.B,
Professor,
Department of Paediatrics,
ESIC Medical College & PGIMSR
Chennai -78

Prof. Dr. Sowmya Sampath
M.D., D.N.B.,
Professor and Head,
Department of Paediatrics,
ESIC Medical College & PGIMSR
Chennai -78

Dean

Prof. Dr. Srikumari Damodaram
M.S., M.Ch(GE)., MAMS., FICS., FACS.,
ESIC Medical College & PGIMSR
Chennai -78

DECLARATION

I solemnly declare that this dissertation entitled **"Serum procalcitonin as a diagnostic marker of bacterial infection in febrile children"** has been conducted by me at ESIC Medical College & PGIMSR, Chennai, under the guidance and supervision of **Prof.Dr.Sowmya Sampath,M.D.,DNB**, Professor and Head, Department of Paediatrics, ESIC Medical College & PGIMSR, Chennai. This dissertation is submitted to **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** in partial fulfillment of the University regulations for the award of the degree of **M.D. Branch VII (Paediatrics)**.

Date:

Place: Chennai (Dr. K. Brindha)

ACKNOWLEDGEMENT

At the outset, I would like to thank my beloved Dean, ESIC Medical College & PGIMSR, **Prof. Dr. Srikumari Damodaram, M.S., M.Ch(GE)., MAMS., FICS., FACS.** for her kind permission to conduct the study at ESIC Medical College & PGIMSR.

I am greatly indebted to **Prof. Dr. Sowmya Sampath, M.D.**, **DNB**, Professor and Head, Department of Paediatrics, ESIC Medical College & PGIMSR, who was my guide for the dissertation. I thank her wholeheartedly for her able guidance and encouragement throughout the study.

I express my sincere thanks to **Prof. Dr. S. Shobhana, M.D., DCH, Prof.Dr.T.L.Ratnakumari M.D., DCH., and Dr.R. Kulandai Kasthuri, M.D., DCH,** former Head, Department of Paediatrics for their strong support and encouragement throughout this study.

I am immensely grateful to **Dr. Henry Suresh David, DCH, Specialist**, Department of Paediatrics, ESIC Medical College & PGIMSR, for his encouragement and suggestions.

I would like to thank the Assistant Professors of the Department of Paediatrics, ESIC Medical College & PGIMSR, **Dr.M.Kumar, M.D, Dr. S. Sathish Kumar, M.D and Dr. C. Sridharan, DCH** for their valuable suggestions for this study.

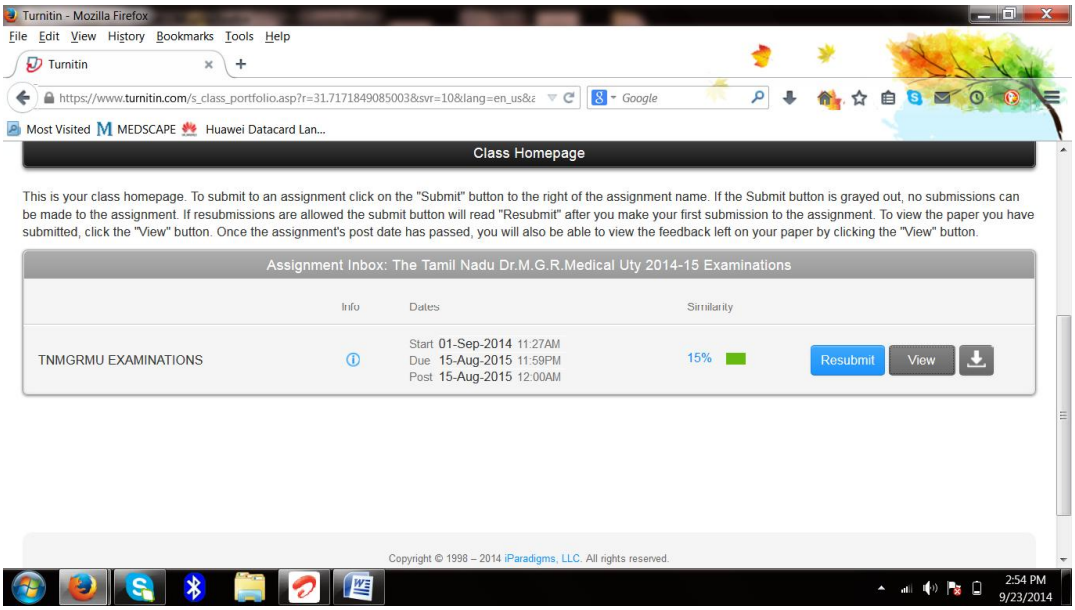
I thank **Dr.Aruna Patil, Statistician**, Department of Community Medicine for her help in the statistical analysis of the study.

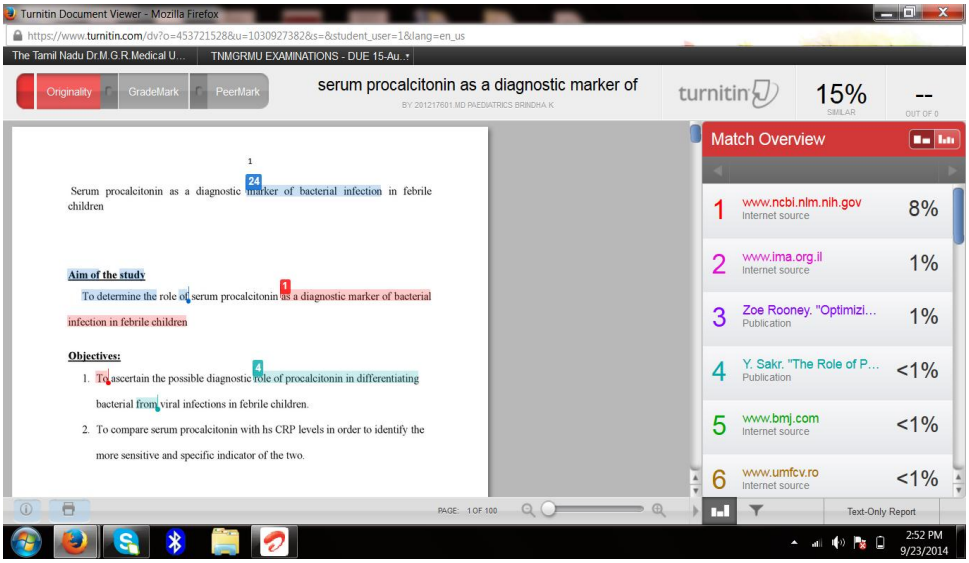
I also extent my sincere thanks to the Departments of Biochemistry, Pathology and Microbiology for their valuable support throughout the study. I will always remember with an extreme sense of thankfulness, the cooperation and criticism shown by my fellow post graduate colleagues & friends.

I would like to extend my gratitude to my beloved family members for their unconditional support in completing my work.

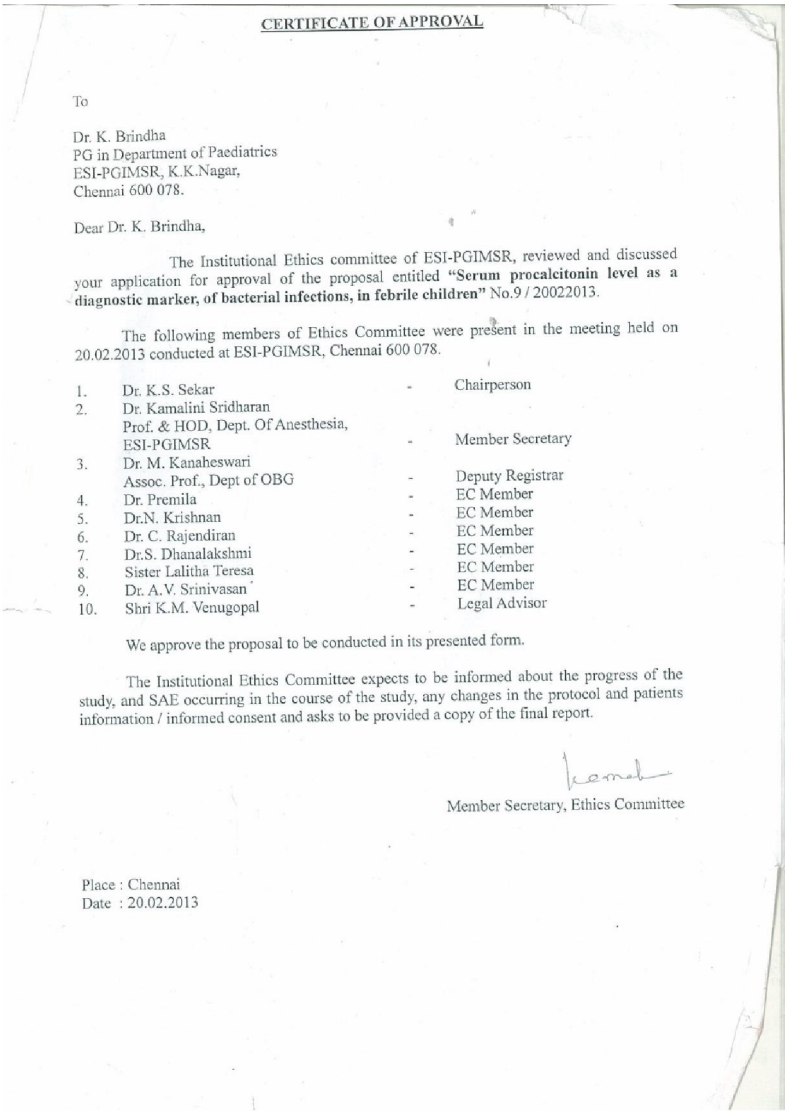
Finally, I wholeheartedly thank the mothers and children, who were the subjects of the study, without whom this would not have become a reality.

Plagiarism check




Turnitin Document Viewer - Mozilla Firefox
https://www.turnitin.com/dv?o=453721528&u=1030927382&s=&student_user=1&lang=en_us
The Tamil Nadu Dr.M.G.R.Medical U...
TNMGRMU EXAMINATIONS - DUE 15-Au..
Originality
GradeMark
PeerMark
serum procalcitonin as a diagnostic marker of
BY 20121760 1.MD PAEDIATRICS BRINDHA K
turnitin
15%
SIMILAR
--
OUT OF 0
1
Serum procalcitonin as a diagnostic marker of bacterial infection in febrile children
Aim of the study
To determine the role of serum procalcitonin as a diagnostic marker of bacterial infection in febrile children
Objectives:
1. To ascertain the possible diagnostic role of procalcitonin in differentiating bacterial from viral infections in febrile children.
2. To compare serum procalcitonin with hs CRP levels in order to identify the more sensitive and specific indicator of the two.
Match Overview
1 www.ncbi.nlm.nih.gov Internet source 8%
2 www.ima.org.il Internet source 1%
3 Zoe Rooney. "Optimizi... Publication 1%
4 Y. Sakr. "The Role of P... Publication <1%
5 www.bmj.com Internet source <1%
6 www.umfcv.ro Internet source <1%
PAGE: 1 OF 100
Text-Only Report
2:52 PM
9/23/2014

Ethical committee approval



CERTIFICATE OF APPROVAL

To

Dr. K. Brindha
PG in Department of Paediatrics
ESI-PGIMSR, K.K.Nagar,
Chennai 600 078.

Dear Dr. K. Brindha,

The Institutional Ethics committee of ESI-PGIMSR, reviewed and discussed your application for approval of the proposal entitled **"Serum procalcitonin level as a diagnostic marker, of bacterial infections, in febrile children"** No.9 / 20022013.

The following members of Ethics Committee were present in the meeting held on 20.02.2013 conducted at ESI-PGIMSR, Chennai 600 078.

1.	Dr. K.S. Sekar	-	Chairperson
2.	Dr. Kamalini Sridharan Prof. & HOD, Dept. Of Anesthesia, ESI-PGIMSR	-	Member Secretary
3.	Dr. M. Kanaheswari Assoc. Prof., Dept of OBG	-	Deputy Registrar
4.	Dr. Premila	-	EC Member
5.	Dr.N. Krishnan	-	EC Member
6.	Dr. C. Rajendiran	-	EC Member
7.	Dr.S. Dhanalakshmi	-	EC Member
8.	Sister Lalitha Teresa	-	EC Member
9.	Dr. A.V. Srinivasan	-	EC Member
10.	Shri K.M. Venugopal	-	Legal Advisor

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study, and SAE occurring in the course of the study, any changes in the protocol and patients information / informed consent and asks to be provided a copy of the final report.

Member Secretary, Ethics Committee

Place : Chennai
Date : 20.02.2013

LIST OF ABBREVIATIONS

PCT	-	Procalcitonin
Hs-CRP	-	highly sensitive C –reactive protein
TLC	-	Total Leucocyte Count
ANC	-	Absolute Neutrophil Count
IL18	-	Interleukin18
PPV	-	Positive Predictive Value
NPV	-	Negative Predictive Value
ROCC	-	Receiver Operating Characteristic Curve
AUC	-	Area Under Curve

CONTENTS

Serum Procalcitonin As A Diagnostic Marker Of Bacterial Infection In Febrile Children

ABSTRACT

Febrile illnesses are the most common cause for seeking health care in pediatric age group. Often children do not have classical signs and symptoms. In the past, various biomarkers have been evaluated with varying degree of sensitivity and specificity in diagnosing bacterial infections. This study aims at ascertaining whether serum procalcitonin (PCT) is able to accurately diagnose bacterial infection among febrile children.The study also attempts to compare the test characteristics of PCT with C –reactive protein (HsCRP) and absolute neutrophil count (ANC). Among the three parameters studied, PCT emerged as a highly specific marker (84.16% specificity), negative predictive value of 89% with an area under curve in ROC (receiver operating characteristic curve) of 0.755. Thus, we would like to postulate that PCT can be used as a single best marker to diagnose bacterial infection in febrile children when used in isolation.

Key words

Procalcitonin, Hs-CRP, absolute neutrophil count,febrile children, antibiotic resistance ,bacterial infection

INTRODUCTION

Acute febrile illness is the most common cause for seeking health care as far as children are concerned. Children do not have definite localizing signs at the time of presentation. Even if there is some localization, it is not possible to differentiate bacterial infection from viral infections based on subtle clinical signs alone [1]. The routine lab investigations on which we rely upon do not entirely differentiate serious bacterial infection from others.

A short overview of certain terminologies is as follows:

Infection:

The invasion of microorganisms and their toxins into normally sterile places, a microbial phenomenon characterized by a definite inflammatory response by the host immune system.

Fever:

It is defined as increased body temperature because of the “reset” of the thermoregulatory mechanism by the hypothalamus. This occurs because of the induction of the host immunity by the cytokines namely INF, IL 6, IL1, TNF etc.

Bacteremia:

Presence of viable bacteria in the host circulating system

In the era of evidence based medicine, definitive treatment like initiating antibiotics needs confirmatory evidence. But waiting for confirmatory reports like culture (blood, urine) is time consuming especially in sick children in whom delay of appropriate treatment can be detrimental. Added to that, most of the time physicians are faced with the difficult task of choosing among a variety of diagnostic tests that are available for the diagnosis of infections in children[2].

A lot of research goes on every year and new tests, for example, those tests based on the polymerase chain reaction[3] (PCR), are increasingly becoming available thereby adding on to the confusion. Many physicians are generally not very familiar with the difficulties in choosing from among the tests and the limitations of many laboratory assays. The interpretation of such test results often changes with reference to the age of the patient and the clinical condition. In the clinical sense, a test employed in the diagnosis, must be timely and cost-effective.

It also must possess appropriate sensitivity and specificity, and the results of that particular test, when they become available, should have a certain amount of impact on the clinical management of the patient's given clinical problem.

The treating physician should be well familiar with the correct techniques for obtaining the sample and also in the transportation of the clinical sample, and in the interpretation of the given results in view of the sensitivity and specificity of that particular assay. On the other hand, indiscriminate use of antibiotics leads to antibiotic resistance[4]

Hence it is high time that we use a biomarker which can reliably differentiate bacterial from other infections, but with acceptable sensitivity and specificity.[5]

In practice, bacterial infections account for 5–25% of febrile illnesses in the pediatric population. The pediatric population hardly shows any localizing signs of infection systemically even in life threatening bacterial infections. It is indeed a big responsibility for the physicians in making an accurate diagnosis of the illness in febrile children and to triage the children who are likely to develop serious complications. Mean while, since children have only self limiting viral illnesses most commonly, care should be taken that they should not be subjected to over investigation and/ or overtreatment.

In the year 2001, the National Institutes of Health (NIH) convened a panel in order to develop standard definitions and a conceptual framework for the discovery of biomarkers and their incorporation into the clinical management .

Based on this consensus definition, a biomarker is broadly defined as follows:

"Biomarker" is a characteristic which can be objectively measured and also evaluated as an reliable indicator of normal biological processes, pathological processes, and/ or pharmacological responses to given a therapeutic intervention. Based on this, biomarkers can be subdivided into two groups,

- "Type 0" and
- "Type 1"

Type – 0 biomarker:

A Type 0 biomarker gives a picture of the natural history of the disease process which correlates with that particular disease in longitudinal manner with known clinical indices & outcomes.

Type 1 biomarker:

A Type 1 biomarker gives a picture of the effects of a therapeutic intervention provided to treat the disease according to its mechanism of action.

"NICE traffic light system"[6] which has been used in diagnosing common bacterial infections has moderate sensitivity but has low specificity in febrile young children. It is used in the detection of common infections namely pneumonia, bacteremia & urinary tract

infections. Many a time's sepsis is a close differential diagnosis of Systemic Inflammatory Response Syndrome (SIRS), especially in very sick children. The differentiation of sepsis from SIRS necessitates a thorough clinical knowledge.

Etiology of SIRS:

SIRS can be of two types:

1) Infectious

2) Non infectious

1) **Infectious causes of SIRS**

- Infections caused by bacteria (pneumonia), viruses, yeasts etc.
- Erysipelas, Influenza
- Infective endocarditis, meningitis, pyelonephritis, appendicitis, cholecystitis, cellulitis, arthritis etc.

2) **Non- infectious causes of SIRS**

- Trauma
- Burns
- Acute pancreatitis
- Poisoning etc.

Sepsis:

SIRS with a documented or suspected infectious etiology

Often distinguishing SIRS (Systemic Inflammatory Response Syndrome) [7,8] from sepsis can be a difficult endeavor since there is a criteria for “infection”. Though infection can be suspected as early as possible at the time of presentation in a given clinical scenario, time duration of 24–48 hours is essential before that suspicion can be confirmed or definitively ruled out by laboratory tests. SIRS can be triggered by a spectrum of non-infectious causes including trauma, transplant rejection, burns, autoimmune/ inflammatory disorders, pancreatitis, graft-versus-host disease etc.

In this particular scenario, “Biomarkers” can be used in the diagnosis, monitoring and to predict the prognosis or the treatment outcome. For many decades, C-reactive protein, which is elevated in inflammatory and infectious conditions, was used as a biomarker indicating infectious conditions worldwide.

SIRS can be diagnosed by the clinical criteria proposed below:

Definition of systemic inflammatory response syndrome [7,8]

The presence of at least two of the following four criteria, one of which must be abnormal temperature or abnormal leukocyte count

- Core temperature of >38.5°C or <36°C
- Tachycardia, defined as a mean heart rate >2 SD above normal for age in the absence of external stimulus, chronic drugs or painful stimuli; OR unexplained persistent elevation over 0.5–4 hour time period; OR in children <1year of age persistant bradycardia, defined as a mean heart rate <10th percentile for age in the absence of external vagal stimulus, β-blocker drugs or congenital heart disease; OR otherwise unexplained persistent depression over a 0.5 – 1hour time period.
- Respiratory rate >2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular disease or the receipt of general anesthesia
- Leukocyte count elevated or depressed for age (not secondary to chemotherapy induced leukopenia) or >10% immature neutrophils.

Even after the use of these clinical criteria, the diagnostic dilemma in differentiating SIRS and sepsis is confounded by the fact that most of the time, those conditions are similar to infectious conditions in their mode of presentation and predispose children to secondary bacterial

infections . In such situations, the use of biomarkers has the potential to help differentiate between the two conditions[8,9].

Infection is defined as the laboratory documentation of a pathogenic organism by positive culture, tissue staining or PCR test, or a clinical syndrome which is associated with a high probability of infection.

Secondly, this differentiation between SIRS and sepsis, is a very essential one from one point as it needs adequate treatment, such as the initiation, selection of appropriate drugs and as a guide in the duration of antibiotic therapy. For the same reason, clinical management guidelines focus primarily on physiologic parameters of well being such as hemodynamic indices, blood oxygen saturations and signs of end organ perfusion.

These indicators give an overall picture of patient status, but they are inadequate in providing accurate real time assessments of the underlying disease condition and they also do not provide essential information for prognostication.

What are biomarkers?

In 2001, the definition of biomarkers was put forth by the NIH special panel. They broadly defined biomarkers as any "characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention." Over the years, so many diagnostic markers for sepsis have been described in literature [8,9]. There are four general types described in recent literature, namely:

- Diagnostic markers
- Monitoring markers
- Stratification marker and
- Surrogate biomarkers

Diagnostic biomarkers:

Diagnostic biomarkers help to establish the presence or absence of a disease state or other clinical condition.

Monitoring biomarkers:

Monitoring biomarkers consist of a group of molecules or proteins that have dynamic variation in the levels, as the disease process evolves or in response to therapeutic interventions. Thus, the medical professional can track the course of disease and can have an ongoing assessment of the adequacy of treatment.

Stratification biomarkers:

Stratification biomarkers are used in the assortment of a group of patients into different varieties based on the disease severity with the intention of applying treatment to groups of patients who will benefit most at the least risk. Stratification biomarkers are used to predict outcome of a disease process rather than follow its course or to titrate therapy.

Surrogate biomarkers:

Surrogate biomarkers serve as proxy end points for severe or rare patient centered outcomes such as death or significant complications.

Various biomarkers and their evolution:

Initial studies employed fever and increased leukocyte counts to define sepsis but these tests were nonspecific[10]. Subsequently, researchers concentrated on erythrocyte sedimentation rate (ESR) and C - reactive protein (CRP) which is also not very specific in diagnosing bacterial infection[9,10]. As we know, sepsis provokes a systemic host immune response inside the body. The knowledge of using the multiple mediators that can be used as biomarkers for both the diagnosis and prognosis of infection became popular. Till date, totally around 180 biomarkers have been evaluated for the same. They include IL-6, lactate, IL-8, soluble triggering receptor which are expressed on myeloid cells-1 (strem-1), and

procalcitonin (PCT)[11]. Procalcitonin has been studied in detail among the other markers, and is supposed to be a promising one.

The use of Biomarkers, on the other hand is supposed to reduce the antibiotic use worldwide[9,10,12]. This in turn can reduce the burden of antibiotic resistance especially in the growing world which has indiscriminate antibiotic usage. India, with population of 1.2 billion, is documented to have one of the highest infectious disease burdens in the world. Due to this alarming rise of drug resistance, biomarkers that help with antibiotic stewardship are needed. Various biomarkers which are used in the infectious conditions are detailed below:

1) Leucocyte count:

Initially, infection was defined by the abnormalities in vital signs and abnormalities in the leukocyte count. But it was found that both leukocyte count & relying on immature forms have low positive and negative predictive values[10]. Also, leukocytosis, was well recognized with noninfectious conditions as well. Hence we do not entirely depend on total leucocyte count as a marker for infection.

2) **CRP:**

CRP is an acute-phase reactant. It is produced only by the hepatocytes in response to any sort of inflammation or tissue injury. The production of CRP is induced by cytokines (IL-1, IL-6 and TNF-α) in response to infection. Serum levels of CRP increase within 4–6 h of an inflammatory stimulus. The concentration of CRP doubles approximately every 8 h from the infectious or inflammatory stimulus and finally peaks at around 36–50 h. It has a very short half life of 4–7 hours [4,9,13].

The median concentration of CRP is below 0.8mg/l and can increase 1,000-fold in healthy young adult volunteer blood donors in response to an acute phase stimulus, Hepatic synthesis of CRP starts rapidly after a stimulus. Since the hepatic synthesis determines the serum concentration, the half-life of CRP is constant under all conditions [4,13].

In pediatric studies, CRP was used in identifying the neonates who have sepsis with non specific clinical signs. It can also be used in other clinical scenarios to distinguish infection from inflammation. It was concluded that using CRP alone lacked the specificity [10,11,13] essential for the discrimination of bacterial, viral and other noninfectious inflammatory conditions.

Due to its poor specificity, CRP is often combined with other biomarkers as part of test panel to assist in the diagnosis of sepsis. CRP can also be used to monitor treatment response once an infectious diagnosis has been established. Most of the recent literature regarding CRP has compared its diagnostic accuracy in diagnosing bacterial infection with that of newer biomarkers, especially the one most spoken of i.e. Procalcitonin (PCT).

3) **CD 64:**

CD64 is a biomarker expressed on the surface of the neutrophils, known as fcγr1. CD64 is one of three receptors on the surface of the neutrophils, whose function is to bind to the fc portion of immunoglobulin (IgG) and thus facilitating opsonization and phagocytosis of the bacteria. CD64 is constitutively expressed at low levels upon the neutrophils. When the immune system encounters an infectious pathogen, the expression of CD64 is highly up regulated. This increased levels of CD64 expression is measured by flow cytometric analysis in the blood samples.

In pediatrics, CD64 has been investigated primarily in the setting of neonatology where it has been used to identify premature and term neonates presenting with sepsis. For the pediatric studies, it was found to have a mean sensitivity of 71% and also a mean specificity of 87% [11]. Some of these studies compared CD64 with CRP or PCT. The results

were conflicting in judging as to whether or not CD64 was a significantly better biomarker. Finally it was concluded that CD64 appeared to be a good marker of infection, across all subgroups when compared with CRP. Importantly, it has to be noted that the methodological quality of the few available studies was poor .

4) **Lactate:**

Serum lactate level is another important biomarker in sepsis, which can be used to distinguish sepsis from septic shock. It is also used in predicting the prognosis of children who are complicated by septic shock. In the past, tissue hypoxia was indicated by serum lactate level. The reduction of serum lactate is accepted as a target for therapeutic interventions in the treatment of septic shock.

Majority of researches with serum lactate have been conducted in adults rather than in the pediatric population where it was concluded that serum lactate was increased in patients with sepsis and patients with increased levels were sicker and had high mortality[11]. So, the reduction of serum lactate is recommended as a target for therapeutic interventions.

5) **IL – 18:**

IL – 18 is a cytokine produced by the activated macrophages participating in the induction of cell-mediated immunity. Literature on

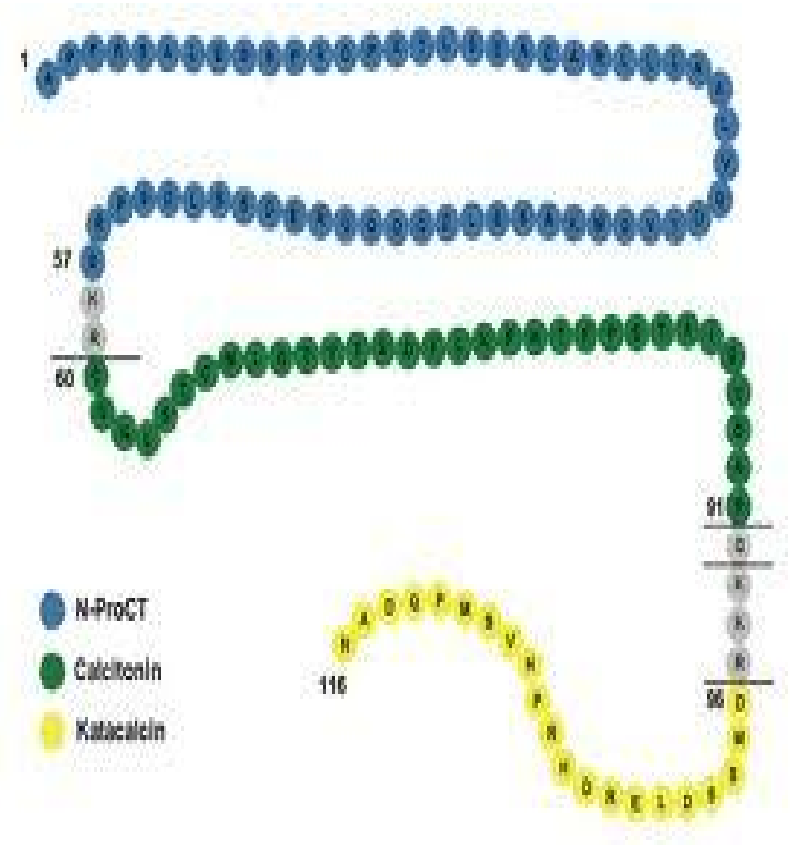
1L-18 is very contradictory[11]. Kingsmore et al, used a high – throughput proteomic immunoassay for the measurement of IL-18 and they, reported that IL-18 is elevated in preterm infants who develop signs and symptoms of sepsis. In another study by Bender et al., they concluded that in neonates IL-18 has diagnostic ability. More research is needed to clarify the utility of this biomarker in the diagnosis and the treatment of sepsis.

Other biomarkers under investigation:

These include novel and interesting markers such as IL-8, CD163, high mobility Group protein b1, urokinase-type plasminogen activator, soluble triggering receptor expressed on myeloid cells and macrophage migration inhibitory factor, etc.

In this current scenario, serum procalcitonin is being used increasingly and is gaining in its application worldwide in the management of infective conditions.

PROCALCITONIN



Schematic representation of procalcitonin

Procalcitonin (PCT), the precursor of the hormone calcitonin which is produced by the C cells of the thyroid gland, is made of 116 amino acids. The normal serum level of procalcitonin is <0.05ng/ml, sometimes it is even undetectable in serum. Half life of procalcitonin is 25-30 hrs in the absence of antibiotic treatment.[14] It is not affected by renal failure, liver failure etc. For some time, it has been recognized that PCT levels are increased in children with sepsis and bacterial infection. Under

normal conditions, the thyroid gland is the only tissue that produces PCT and serum levels are very low. Although the exact proximal stimuli that mediate PCT secretion are unknown, evidence suggests that early inflammatory signals such as TNF-α, IL-1β and IL-6 play a role.[15,16]

Serum levels are increased in response to pro inflammatory stimuli i.e. bacterial endotoxins by the induction of calc-1 gene expression. There after procalcitonin rises in the serum within 2-3 hours of induction. The rate of rise is 0.5ng/ml and plateau is attained in 6-12 hours. With the initiation of appropriate antibiotic therapy, the level of procalcitonin falls to the baseline within 48hours of treatment. Assicot et al. demonstrated that the site for production of procalcitonin during inflammatory processes can either be the liver or the lungs.

In vitro studies were carried out using various cells, namely, monocytes, endothelial cells, polymorphonuclear cells and macrophages, which were stimulated with endotoxin following which the production of procalcitonin was studied. The pattern of its production is in the similar manner as that of some components of the cytokine cascade activation system, and some markers involved in the activation of cellular immunity[13,15].This observation suggests that procalcitonin is an acute-phase inflammatory reactant.

In the animal studies, a trial administration of a supra physiologic amounts of procalcitonin caused an increased mortality in experimental sepsis in an animal model. On the other hand, prophylactic and

therapeutic immune blockade of the pathway of procalcitonin secretion using multiregion -specific goat antiserum reactive to procalcitonin resulted in increased survival.

In neonates, Procalcitonin is a good marker for detecting sepsis. Increased levels of procalcitonin were found in all neonates with bacterial sepsis, whereas babies with viral infection or bacterial colonization had normal levels or only slightly increased levels which were insignificant. In the diagnosis of early-onset sepsis, procalcitonin levels has a sensitivity of 92.6% and specificity of 97.5%[14] which is acceptably good compared to all other biomarkers used in the newborn period.

Estimation of serum procalcitonin is helpful in differentiating infection from autoimmune diseases with active disease process. In such children, procalcitonin can serve as an important tool because patients with autoimmune diseases are prone to serious infection, particularly under conditions of iatrogenic immunosuppression.

For all of the above advantages, procalcitonin can be used as a sensitive marker for diagnosing bacterial infection in children presenting with acute febrile illness without localizing signs. It can also be used as a prognosticating marker for guiding antibiotic treatment[17]. Additionally, when the patient responds appropriately to therapy, PCT levels return to normal much quicker than CRP.

Simon et al. measured PCT and CRP levels in 64 children who developed SIRS and compared values between those with a positive confirmation of infection and those without. Those with confirmed

infection (sepsis) had significantly higher PCT values than those without (SIRS only), but CRP levels did not differ between the two groups. The area under the curve for PCT in that study was 0.71 versus 0.65 for CRP[13].

Arkader et al. demonstrated that in children with sepsis, serum PCT concentration was significantly high above that of non infected children with SIRS following cardiopulmonary bypass surgery which had (AUC: 0.99). In this setting, however, CRP could not distinguish the two states,namely sepsis and systemic inflamatory response syndrome (AUC: 0.54). In a group of 359 children cared for in a pediatric intensive care unit, Rey et al. showed that PCT was much more superior to CRP in distinguishing six classes of patients: those without SIRS or sepsis; SIRS alone; localized infection; sepsis; severe sepsis; and septic shock and the definitions of each class is well defined in the study. Procalcitonin levels were significantly high with respect to the severity of illness (AUC: 0.91), but CRP failed to detect the trend of the response to treatment as good as procalcitonin (AUC: 0.75).

The literature search regarding the use of procalcitonin for the children who had burns and in whom sepsis was suspected was made.

Only very few studies have been conducted regarding the use of procalcitonin in burns children.

As burns also triggers an inflammatory response, sometimes as severe as SIRS, the use of reliable biomarker is needed for the same. Neely et al in 2004 studied the use of procalcitonin as an early marker of sepsis in pediatric burns. Though the definition of sepsis was not defined in a clear manner in this study, their results showed that the cut off for procalcitonin in the diagnosis of bacterial infection is same as for general population.

Serial measurement of PCT levels has also been used as a monitoring biomarker to direct and limit antibiotic usage. The purpose of this application is to reduce bacterial antibiotic resistance as well as patient-centered side effects such as nephrotoxicity and drug reactions[17]. In the past procalcitonin had limited usage in pediatrics.

To date, there has been no single biomarker discovered that offers clinicians, caring for sick children, the absolute diagnostic ability to distinguish sepsis from other inflammatory [18,19]disorders or to monitor and predict its progression or response to treatment.

Likewise, markers for septic shock are inadequate and limited in their utility. It is unlikely that any single biomarker will be able to predict with complete certainty the presence or absence of a disease or of a specific outcome.

All biomarkers must be used in their appropriate clinical context as adjuncts to the decision-making process. That being said, however, the use of serum PCT levels appear to be a significant improvement over CRP that has traditionally enjoyed broad historical usage.[20] PCT has been shown, to our satisfaction, to improve the ability of clinicians in diagnosing, monitoring and predicting outcome in both sepsis and septic shock.

AIMS AND OBJECTIVES

AIM OF THE STUDY

- To determine the role of serum procalcitonin as a diagnostic marker of bacterial infection in febrile children.

OBJECTIVES

- To ascertain the possible diagnostic role of procalcitonin in differentiating bacterial from viral infections in febrile children.
- To compare serum procalcitonin with hs CRP levels and ANC in order to identify the more sensitive and specific indicator of the two.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

This study aims at finding out as to whether procalcitonin can be used as a marker for diagnosing acute bacterial infection in febrile children and to compare it with Hs-CRP to find the more sensitive/ specific marker among the two.

The procalcitonin level in serum was found to be closely related to severe invasive bacterial infection and SIRS. When the infection is loco-regional or confined to a single organ in the absence of systemic response of the inflammatory reaction, the procalcitonin is low or only moderately increased. It also remains low in viral infection. Several studies were made in the past, determining the effect of serum values of Procalcitonin, Hs CRP and absolute neutrophil count (ANC) both singly and in combination[18-24]. Based on these, some of the biomarkers are included in the algorithm used in sepsis management.[25]

Procalcitonin:

In 1993, Assicot et al[26] studied the use procalcitonin in differentiating viral and bacterial meningitis. They found that Procalcitonin in serum increases in bacterial meningitis. Their study yielded a sensitivity of 99% and a specificity of 100%. In 1994, Dandona et al[27] documented an increase of procalcitonin levels in the sera of normal individuals after injecting endotoxin. Thus, they concluded that the level of PCT rises with septicemia and in normal subjects this does

not occur. In 1999, Vialon et al studied the same effects of the rise of procalcitonin in adults with meningitis. They also found that serum procalcitonin rises in adults with meningitis and this supports the observation made by Assicot et al.

Craig et al[28] initially studied the diagnostic value of clinical symptoms and signs in the diagnosis of bacterial infection in young children with fever. According to his study, the diagnosis of bacterial illness by the physicians had a very low sensitivity (10-50%) but high specificity (90-100%). Several important red flags were identified in the diagnostic value of presenting clinical features in identifying serious infections in children.

Use of symptoms and signs alone often resulted in uncertainty in the diagnosis with the risk of under diagnosis of severe infections. Thus, the biomarkers are essential for the reliable distinction of bacterial infection. They also help in decisions to admit or not, to start antibiotics or not and also when to stop or change. The concentration of serum PCT sensitive enough to diagnose bacterial meningitis was studied by Jereb et al[29] in 2001. They found the predictive value of procalcitonin in CSF and serum to be >0.5ng/ml as reliable cut offs with high PPV and NPV, in relation to bacterial meningitis. In the same year, Giamarllos et al[30], evaluated the role of procalcitonin as a diagnostic marker in children with febrile neutropenia . From their study, they concluded that values more than 2 ng/ml indicate definite evidence of systemic infection.

In the newborns, procalcitonin is supposed to be a reliable tool in differentiating bacterial and viral infection. Controversy exists in the literature as it whether procalcitonin or Hs CRP is a best tool in the detection of newborn sepsis. Some authors demonstrated that procalcitonin lacked sensitivity and specificity in within the newborn age group.

This might be due to the fact that procalcitonin can have variable kinectics in the perinatal period. There is a physiological surge of serum procalcitonin approximately 24 hours of life which returns to normal after third day of life. Hence there are age related nomograms developed for preterm babies.

In 2001, Connor et al[31] first described the use of PCT in the prognostication of bacterial infection. They also found that PCT differentiates infectious causes of SIRS from non infectious causes which are very essential from the treatment point of view. In 2003, Colombier et al used quantitative measurement of PCT values for the diagnosis of bacterial infection. They concluded that PCT values more than 1.2ng/ml is definitely associated with bacterial infection and thus it can be used to guide the antibiotic therapy in hospital settings. Mirjanichrist et al, in 2004, did a study incorporating the role of PCT in the etiologic diagnosis of lower respiratory tract infection. They described the role of PCT as a diagnostic marker in lower respiratory tract infection, thereby reducing

antibiotic abuse and suggested the use of a PCT based algorithm in guiding antibiotic treatment.

In 2005, Oberhoffer et al[32] studied the role of biomarkers in infectious states. The study was done to predict the outcome by the traditional and new markers of inflammation in patients with sepsis. They concluded that PCT appears to be a more accurate marker than its counterparts namely, hs-CR, counts, temperature etc. among the other markers of inflammation.

The role of PCT and its kinetics, were studied by many authors. In 2005, Yukioka et al[33] concluded that PCT is the earliest marker to rise and the level of rise indicates the severity of infection. Authors then began investigating the out performance of PCT compared to other inflammatory markers.

In 2006, David Herd et al[34] carried out a study in children presenting with fever, in which it was noted that though PCT can be used to differentiate bacterial from other illnesses, he concluded that PCT, when used alone is not a very sensitive indicator. Dauber et al[35] in 2008, stated that although PCT values show mild increase in vaccinated children, it can still be used to differentiate this from infectious causes of fever. In the same year, Maniaci et al[36] studied the role of PCT in young children and concluded that in young babies, who often do not have localizing signs, PCT can be used to detect occult bacterial infection.

Baer et al[37] in 2010, compared CRP and other biomarkers and found that PCT emerged as a single best marker in the molecular diagnosis of sepsis. Schutz et al in 2011[38], investigated the use of PCT based algorithm in the diagnosis and treatment of various diseases. They found that PCT determination, as a guide, reduces the use of antibiotics considerably.

Thus in end of the previous decade the use of procalcitonin became widespread worldwide in diagnosing bacterial infections though data is limited as far as our country is concerned. In a study conducted by Micheal Baer et al, in 2010, they foung PCT is the best biomarker among all the available biomarkers currently which was in othedies. The study group concluded that this algorithm is useful in severe sepsis, post operative infections and severe sepsis.

In the Cochrane review, 2012, on the role of PCT to initiate or to discontinue antibiotic treatment, it was concluded, there is no increased mortality, and in turn there is a significant reduction of antibiotic consumption.

Hs-CRP and Absolute neutorphil count(ANC) The role of hs-CRP in bacterial or viral infection is well known but it does not differentiate bacterial infections from other infections. It rises in other inflammatory conditions as well. CRP is known to rise in non inflammatory conditions as well. Derek et al [39] in 2000, tried to correlate the concentration of CRP with adiposity in children. The study showed a strong correlation of CRP with adiposity in children with a statistical significance of P <0.0006. In 2003, Prat et al , evaluated the role of CRP, TLC and PCT in lower respiratory tract infection in children.

They also concluded from the study that PCT showed a positive correlation with the etiology of respiratory tract infection when it was due to bacteria. Both CRP and procalcitonin show high sensitivity for distinguishing pneumococcal etiology from other infective etiologies. Among both, PCT shows a higher specificity than CRP. This was further supported by Gendrel et al[40] who investigated the relation between procalcitonin and CRP and INF& IL 6.PCT >1 mg/l is more sensitive and specific compared to CRP, IL-6 and INF. Brauner et al in 2009[41], studied the role of leucocyte count in predicting bacterial infection. It was found that elevated WBC counts >25,000 cells were associated with serious infections in the 3 – 36mo age group, most commonly pneumonia. Similarly, in another study by, Ayazi et al in [42]2009, they studied the diagnostic accuracy of ANC and CRP in diagnosing bacterial illness.

ANC and CRP were neither specific nor sensitive in diagnosing bacterial infection of urinary tract. Recently in 2014, Elemraid et al studied inflammatory markers in diagnosing the etiology of pneumonia. Bacterial pneumonia had high CRP >80mg/L and levels <20 mg/L were inconclusive in finding the etiology.

Ann Van den Brue et al in 2011, studied the diagnostic accuracy of the tests in identifying bacterial illness.WBC counts are not useful in the diagnosis of bacterial illness. They also suggested the use of different cut off values for ruling out or ruling in the infections. In the review study and meta analysis done by Simion et al, comparing PCT and Hs-CRP levels as a marker of bacterial infection, PCT was concluded to be a more sensitive and specific marker than Hs-CRP in diagnosing bacterial infection.

The evidence for PCT turning into the best among the biomarkers identified is increasing. Rui-ying Xu et al[43], in 2014, analysed the diagnostic accuracy of procalcitonin and C-reactive protein in diagnosing the degree of renal involvement. PCT values were raised with more severe degree of renal involvement and the CRP did not correlate with the degree of renal involvement.

Among the other predictors of bacterial infections, total and absolute leucocyte count deserves a special mention. Al-majali et al[44], in 2004, in children of age 1-18 months with fever, studied the relationship

between white blood cell and absolute neutrophil count. They arrived at a conclusion that ANC predicts bacterial infection accurately in young children with fever without focus.

Saskia et al in 2013[45], studied the characteristic features of serum C reactive protein and procalcitonin measurements along with symptoms and signs in the diagnosis of pneumonia. They also found that adding CRP concentration >30 mg/l has diagnostic value but procalcitonin values does not correlate with diagnosis of pneumonia clinically.

In 2001, Moulin et al[46], found that PCT values, with a threshold of 1 ng/ml has high sensitivity and specificity and PPV and NPV than CRP, IL 6, and WBC in the differentiation of bacterial pneumonia and viral pneumonia.

Chia-hung Yo et al[47], in 2012, concluded that procalcitonin can be used for ruling out bacterial infection than for ruling in the same. They also found that though there is a lot of data on procalcitonin, prevailing evidence does not show how procalcitonin can be combined with other clinical data.

In the same year, Nabulsi et al[48], studied the evidence-based decision-making in bacterial illness by CRP. They also suggested better quality research is essential for the definitive determination of the diagnostic accuracy of CRP levels in children. The present evidence for

CRP in children with bacterial infection is weak and has low diagnostic value.

PCT for Antimicrobial Stewardship

Due to its ability to help differentiate between viral and bacterial infections, PCT has been evaluated for its ability to guide decisions for appropriate antibiotic therapy.

India has one of the highest rates of infectious diseases and has alarmingly high rates of resistant bacteria, making utilization of diagnostics that help indicate when unnecessary antibiotics can be avoided, as a prime goal.

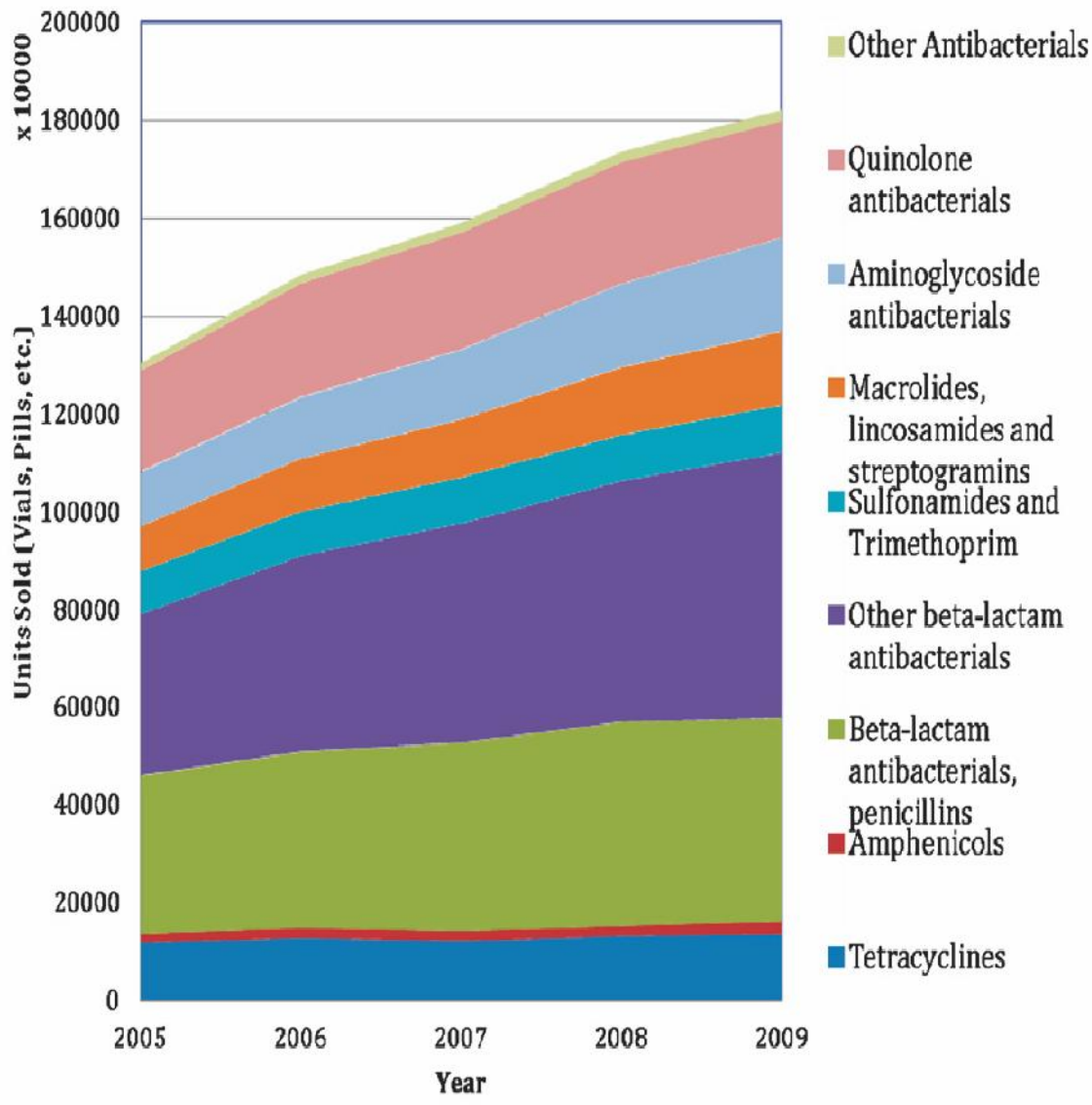
The PRORATA trial, a multicenter, prospective, open-label, and randomized control trial including 621 patients in 8 ICUs in 6 hospitals followed these smaller studies and found a 23% reduction in antibiotic usage at day 28. There are a lot of studies in literature showing the rising antibiotic resistances in the community, especially in a growing country like India though the pediatric studies are limited. There are a lot of working group formulated algorithms including diagnostic parameters in the initiation of antibiotic treatment to reduce drug resistance.

In 2005, Oosterheert et al[49] studied whether increased diagnostic modalities can overcome the problem of antibiotic resistance. Utilization of RT- PCR for the etiological diagnosis of lower respiratory tract infection, increased the diagnostic accuracy, but antibiotic use was

unaltered. In 2007, Mohammed Akram et alwhile studying the resistance pattern of bacteria in India, studied an increasing resistance to co-trimoxazole and production of extended spectrum β-lactamase among the bacteria causing UTI in the community.

D Raghunath et al[12] in 2008, suggested the development and evaluation of improved diagnostic methods for diagnosing bacterial infection. As per Global Antibiotic Resistance Partnership (GARP) - India working group*- current antibiotic trend in India's suggests increasing the use of diagnostic tests as one of the measures to reduce antibiotic usage and resistance.

As per our recent evidence, Adnan Mannan et al[50] in 2014, studied bacterial resistance patterns in India, 64.2% of S. typhi were multidrug resistant. Thus, it is high time we cut down the antibiotic consumption based on evidence based medicine. In 2014, Nelson et al[5] reviewed sepsis biomarkers with special reference to the Indian scenario. PCT ay be used as a tool in the sepsis algorithm. It also lessens dependence on microbiology resources in India.



This picture illustrates the increasing use of antibiotics in India[21]. The volume of consumption of antibiotics has also increased from 2005 and is still on the increasing trend. Also, the rate of use of higher antibiotics can be increasingly noted. This is because of the increase in the resistance pattern of the pathogens causing bacterial illness to the common drugs[51]. This alarming increase in drug resistance could be partly due to the inadvertent and indiscriminate antibiotic usage by the medical professionals [52,53]. Though there are many reasons for this trend

of antibiotic prescription, like lack of knowledge for choosing an appropriate drug for the particular disease, one of the main reasons could be lack of appropriate diagnostic skills[54].

The use of RT-PCR for diagnosing respiratory pathogens causing lower respiratory tract infections has involved higher cost in the diagnosis and management[54]. At the same time it does not cause any reduction in the antibiotic use by the physicians. Hence we need a simple and cost effective diagnostic tool which can be used in the emergency department, well capable of diagnosing bacterial illnesses with acceptable sensitivity and specificity.

CRP is sensitive enough in diagnosing bacterial illness but has low specificity in ruling out the infections when the infection is not severe. This again will not be a better guide in starting on antibiotics, giving the benefit of doubt.

Procalcitonin when used in the emergency department can reliably used in the diagnosis of bacterial illness in children. Based on that, the primary physician can make an evidence based decision for initiating antibiotics. Various meta analyses recommend the use of procalcitonin based algorithms in the initial diagnosis and the management of sepsis.

MATERIALS AND METHODS

MATERIALS AND METHODS

Place of study

Department of Paediatrics, ESIC Medical College & PGIMSR, K.K Nagar, Chennai

Study design:

Prospective descriptive study

Study period:

From February 2013 - October 2014

Study population:

All children (6 months to 12 years of age) admitted to the Department of Paediatrics at ESIC Medical College & PGIMSR, K.K Nagar, Chennai, with an acute febrile illness (temperature >100.4º F), were enrolled in the study. An informed written consent was obtained from their parents. A detailed history was recorded along with complete clinical examination in a proforma. Provisional diagnosis was the one made by the admitting physician. This was subsequently revised after completion of the investigations

Inclusion criteria:

- Children > 6 months with an acute febrile illness (< 14 days duration) with a temperature of >100.4º F

Exclusion criteria:

- Children who had received antibiotic treatment within 48 hours of presentation to hospital
- Children with collagen vascular disorders
- Children with severe trauma
- Children with burns
- Children with major surgery
- Children with prolonged shock
- Immunocompromised children
- Children vaccinated during the previous 48 hours

Investigations:

All children recruited were subjected to the following investigations:

- Complete blood count
- Peripheral smear
- Procalcitonin
- Hs CRP
- Blood culture
- Dengue serology
- Urine routine examination
- Urine culture
- Chest X ray

Lumbar puncture with CSF analysis was performed as and when the clinical situation mandated it.

Methodology:

2ml of blood was taken from the peripheral vein in a heparin coated test tube for Hs-CRP and PCT estimation

Procalcitonin (PCT):

PCT was measured using BRAHMS – PCTQ semi quantitative assessment kit. Labeled blood samples were collected and sent from the

ward to the laboratory. Both the hospital insurance number and the inpatient number were written on each of the samples to avoid confusion. Samples were then centrifuged at the rate of 3500 rpm for three minutes and the serum was allowed to separate.

Execution:

The individual test package was not opened until immediately prior to running the test. 6 drops of the serum (200 microlitres) was pipetted, using the enclosed dropper pipette, and introduced into the round cavity of BRAHMS PCT – Q kit and the rest of the sera were disposed. The kit was incubated for 30 minutes at room temperature. After 30 minutes, procalcitonin concentration range of the sample was determined. At first, the validity of the test was ascertained with the clearly visible control band on the kit. The procalcitonin concentration range was then determined by comparing the colour intensity of the test band with the colour blocks on the reference card and documented as <0.5ng/ml or >0.5 ng/ml.

This BRAHMS PCT – Q kit has a sensitivity of 90 – 92% and a specificity of 92 – 98% compared to other methods of estimation. The PCT – Q is marketed as a point – of – care testing kit. Results are indicated by four different shades of red, corresponding to different PCT ranges, indicating the possibility and also the severity of sepsis.

Labeled BRAHMS PCT Q Kit with PCT estimation

Hs – CRP:

Labeled blood samples were sent from the pediatric ward. These were subjected to centrifugation at 3500 rpm for 3 minutes and the sera were allowed to separate. The serum was then added to the automated hs CRP analyser. Various assay methods are available for CRP determination, such as nephelometry and turbidimetry.

We used Roche/Hitachi **Cobas C** systems for the estimation of hs CRP. The Roche CRP assay is based on the principle of particle – enhanced immunological agglutination.

Test principle:

Particle enhanced immuno – turbidimetric assay

Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The precipitate is determined turbidimetrically.

Lower detection limit:

0.15 mg/L

Method of estimation of Hs CRP

Total and absolute neutrophil count estimation:

2ml of blood was taken in EDTA coated test tube, under aseptic precautions, and sent to the laboratory with proper labeling. Total count was analysed using Cobas C 5 part automatic cell count analyser. Results which were displayed were noted down. The quality control for the analyser was run once every day.

Machine used for the estimation of total count

From the total leucocyte count and the percentage of neutrophils in the differential count, the absolute neutrophil count (ANC) was derived using the formula given below:

$$ANC = \frac{\text{Percentage of Neutrophils X Total Leucocyte count}}{100}$$

Blood culture:

1 ml of blood was taken under strict aseptic precautions in liquid culture media (BHA broth) and incubated for 72 hrs in blood agar and Mac conkey agar for the growth of any pathogenic organisms.

Urine culture:

5ml of urine is collected, by mid stream clean void, in a sterile test urine container and incubated in Hi Chrome culture media. Results were read after 24 hours for possible growth of organisms.

Results were documented for each patient and appropriate treatment was initiated, as per the department's standard protocol once the final diagnosis was arrived at.

Statistical analysis

The results of procalcitonin, hs – CRP and absolute neutrophil count were compared and analysed using pearson chi square method. The diagnostic accuracy of all the parameters was then compared and interpreted with reference to clinical data.

In the present study, the statistical methods were for quantitative data, descriptive statistics was presented by N, Mean, Standard Deviation and Range. For qualitative data, frequency count, N and percentage were put in a tabular manner.

To analyze the data, an appropriate statistical test was applied so as to find the association between parameters, Chi square test (2x2 cross tabulation) was used. Screening tests such as Sensitivity, specificity, ROC curve have been calculated.

All the statistical analysis has been done by using statistical software SPSS (version 16.0). Other data, displayed by various tables and charts, were done by using Microsoft excel (windows 7).

* Significant at $p < 0.05$

** Very significant at $p < 0.01$

*** Highly significant at $p < 0.001$

The diagnostic accuracy of each parameter was also assessed by calculating its area under receiver operating characteristics curve (AUROCCs), which was plotted for the three main markers of infection namely procalcitonin, hs CRP and ANC. AUROCC is a validated way to measure the diagnostic accuracy of a test or the discriminatory power of a prediction rule. AUROCC values can have a range from 0.5 to 1.0 wherein a value of 0.5 would indicate a test that is of little use while a value of 1.0 would indicate a perfectly discriminatory test. In practice, a test with an AUROCC value of less than 0.75 would not be considered as contributory.

OBSERVATIONS AND RESULTS

OBSERVATIONS AND RESULTS

TABLE-1

GROUP CHARACTERISTICS

Character	**No. of cases [n (%)]**
0-5 years	103 (60.1%)
6-12 years	155 (39.9%)
Male	158 (59.7%)
Female	108 (40.3%)
Fever <7 days at presentation	241(93.3%)
Fever >7 days at presentation	17 (6.6%)
No. of cases with procalcitonin	258 (100%)
No.of cases with CRP	258 (100%)
No.of cases with ANC	258 (100%)
No.of cases with blood culture	152 (58.9%)
No.of cases with urine culture	122 (47.2%)

INDIVIDUAL PARAMETERS

Table 2

Age distribution of the study population

Study population	0 – 5 years	6 – 12 years
258	103	155

Total no. of cases – 258

Children in age group 0 to 5years – 103

Children in age group 6 to 12 years – 155

Fig. 5: Age distribution

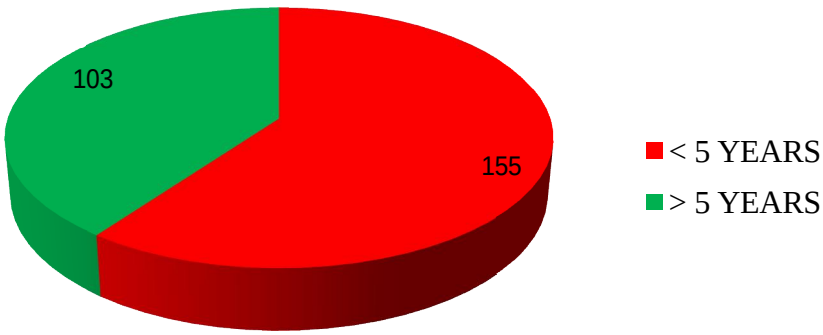


Table – 3

Association between levels of serum procalcitonin and age group

	Procalcitonin(ng/ml)			**Pearson Chi-Square value, df**	**P value**
Age (years)	< = 0.5	> 0.5	Total	0.889 (a),1	0.346
0—5	118 (61.8%)	37 (55.2%)	155 (60.1%)		
5—12	73 (38.2%)	30 (44.8%)	103 (39.9%)		
Total	191 (100%)	67 (100%)	258 (100%)		

An attempt was made to compare the levels of procalcitonin in children less than 5 years and older children to look for any significant differences, as it is a well known fact that elevated PCT levels may be an indicator of severe bacterial infections in younger children. In both the age groups, 0 – 5 yrs and 5 – 12 years it is not statistically significant.

Table –4

Sex distribution of the study population

Study population	Male	Female
258	150	108

Total number of cases – 258

No. of male children – 150

No. of female children – 108

Male:female–1.4:1

Fig. 6: Sex distribution

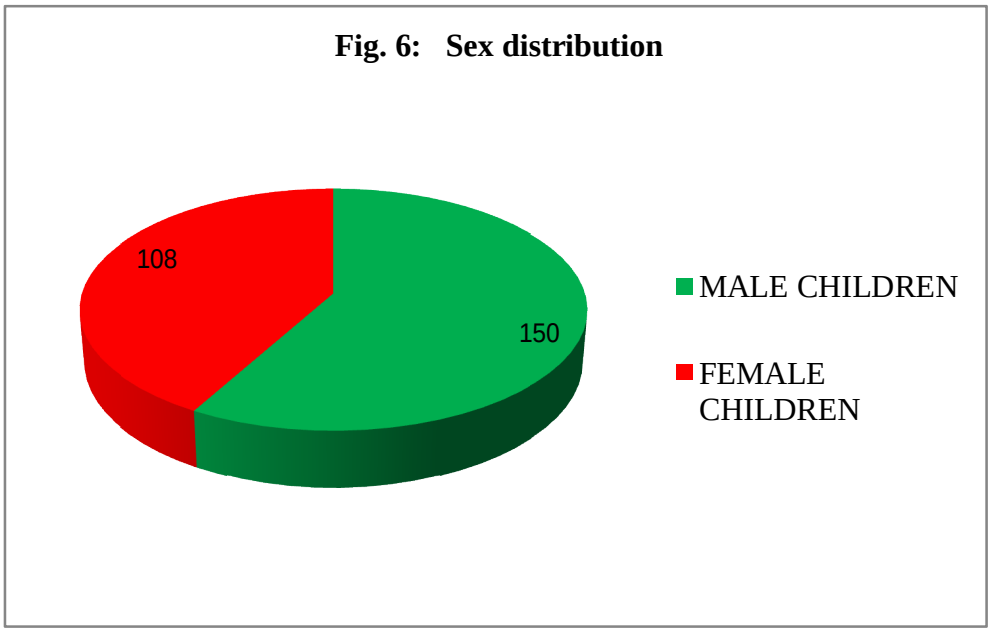


Table – 5

Association between serum procalcitonin and gender:

	Procalcitonin(ng/ml)			**Pearson Chi-Square value, df**	**P value**
Gender	< = 0.5	> 0.5	Total		
Female	78 (40.8%)	26 (38.8%)	104 (40.3%)	0.085 (a),1	0.771
Male	113 (59.2%)	41 (61.2%)	154 (59.7)		
Total	191 (100%)	67 (100%)	258 (100%)		

There appear to be no significant differences in the procalcitonin levels among boys and girls. The pearson chi square value is not statistically significant.

Table – 6

Proportion of bacterial and viral infections in the study population

Study population	Bacterial infections	Viral infections
258	56	202

Total no. of cases – 258

No. of cases diagnosed with bacterial infection* - 56

No. of cases diagnosed with viral infection – 202

Viral infection: bacterial infection – 3:1

*Bacterial infection proven by the growth of pathogen in blood/ urine/ other body fluids and diseases known to have been caused by bacteria most commonly, though confirmatory evidence is not obtained, like pneumonia

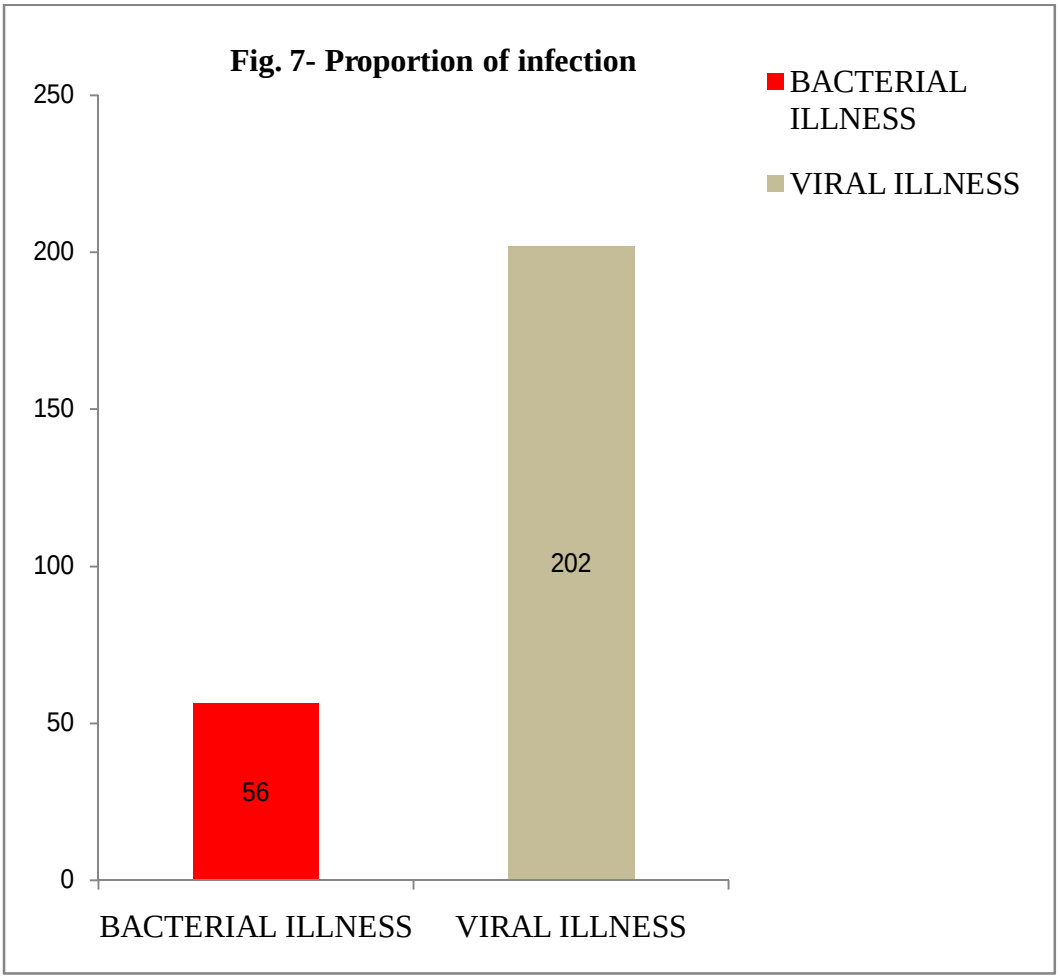


Fig. 7- Proportion of infection
BACTERIAL ILLNESS
VIRAL ILLNESS
250
200
150
100
50
0
56
202
BACTERIAL ILLNESS
VIRAL ILLNESS

Table – 7

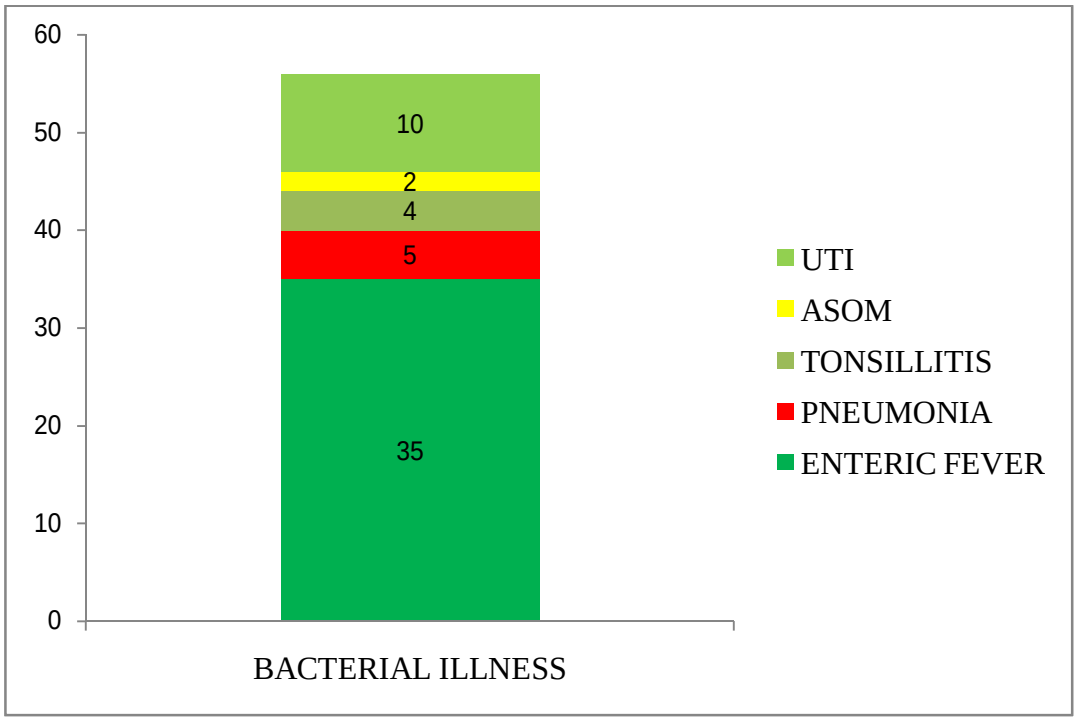
Bacterial infections in the study population

Study population	Enteric fever	UTI	Others
56	35	10	11

Of the total 56 cases with bacterial infections, 62.5% had enteric fever, 17.1% had UTI and remaining 19.6% had other bacterial infections.

Fig. 8

Bacterial infections in the study population



Total no. of cases diagnosed with bacterial infections – 56

Enteric fever – 35

Urinary tract infection – 10

Pneumonia – 5

Tonsillitis – 4

Acute suppurative otitis media (ASOM) – 2

Table – 8

Clinical characteristics Association between total duration of fever and serum procalcitonin levels

	Procalcitonin(ng/ml)			**Pearson Chi-Square value, df**	**P value**
Fever (days)	< = 0.5	> 0.5	Total		
Up to 7	178 (93.2%)	63 (94%)	241 (93.4%)	0.056 (a),1	0.812
Above 7	13 (6.8%)	4 (6%)	17 (6.6%)		
Total	191 (100%)	67(100%)	258(100%)		

In the two groups i.e. fever <7 days and > 7 days, the degree of rise of procalcitonin does not correlate with the duration of fever. The pearson chi square test for this is not statistically significant, P >0.5.

Table – 9

Association between day of defervescence of fever and serum procalcitonin values

	Procalcitonin(ng/ml)			**Pearson Chi-Square value, df**	**P value**
Fever defervescence (days)	< = 0.5	> 0.5	Total		
<=5	179 (93.7%)	57 (85.1%)	236 (91.5%)	4.75 (a),1	0.029*
>5	12 (6.3%)	10 (14.9%)	22 (8.5%)		
Total	191 (100%)	67(100%)	258(100 %)		

Among 22 children who defervesced after 5 days of admission, 14.9% cases had procalcitonin levels more than 0.5ng/ml. This association is statistically significant with $P < 0.05$ ($P = 0.029$)

Table-10

Association between serum procalcitonin and final diagnosis

	Final diagnosis			**Pearson chi-square value, df**	**P value**
Procalcitonin (ng/ml)	Bacterial infections	Viral infections	Total		
< 0.5	21 (37.5%)	170(84.2%)	191 (74%)	49.649(b), 1	<0.0001***
> 0.5	35 (62.5%)	32 (15.8%)	67 (26%)		
Total	56 (100%)	202 (100%)	258 (100%)		

Procalcitonin values obtained were grouped into two, namely, < 0.5 ng/ml and >0.5ng/ml. Of the total 56 cases with bacterial infections, 35 cases had serum procalcitonin values >0.5ng/ml (62.5%). Thirty two cases with viral illness had (15.5%) procalcitonin values >0.5%.

Remaining 170 cases (84.2%) had procalcitonin values <0.5ng/ml. This indicates a strong association between high serum procalcitonin values and bacterial infections ($p<0.0001$).

Table – 11

Association between blood C/S and serum procalcitonin

	Procalcitonin(ng/ml)			**Pearson chi-square value, df**	**P value**
Blood c/s	< = 0.5	> 0.5	Total	22.864(b) 1	<0.0001 ***
Positive	12 (6.3%)	19 (28.4%)	31 (12%)		
Negative	179 (93.7%)	48 (71.6%)	227 88%)		
Total	191 (100%)	67 (100%)	258 (100%)		

Of the total 56 cases with bacterial infection, 35 cases had enteric fever. 31 cases were culture positive; 19 cases with PCT >0.5ng/ml had blood culture positivity (28.9%) and 48 cases with culture negativity also had PCT >0.5ng/ml (71.6%). The P value for this observation is <0.0001* which is highly significant i.e. there is a strong association between culture positive cases and PCT >0.5ng/ml. Of the total 191 cases with PCT <0.5ng/ml, 171 cases had culture negativity and 12 cases had culture positivity who turned out to be enteric fever.

Table – 12

Association between urine c/s and serum procalcitonin

	Procalcitonin(ng/ml)			**Chi square (continuity correction(b)) value, df**	**P value**
Urine c/s	< = 0.5	> 0.5	Total	15.962,1	<0.0001***
Positive	1(0.5%)	8 (11.9%)	9 (3.5%)		
Negative	190 (99.5%)	59 (88.1%)	249 (96.5%)		
Total	191 (100%)	67 (100%)	258 (100%)		

A total of 8 urine culture positive cases (11.9%) had PCT values >0.5ng/ml and only one case has the PCT <0.5. Of the total of 249 cases with negative urine culture, 190 cases (99.5%) had PCT <0.5ng/ml and only 59 cases had PCT (88.9%). As per the pearson chi square test, the P value is <0.0001 *** and this association is highly significant statistically.

Table –13

Evaluation of serum procalcitonin as a diagnostic test

Parameter	Estimate	Lower - Upper 95% confidence intervals	Method
Sensitivity	62.50%	(49.41, 73.99)	Wilson score
Specificity	84.16%	(78.49, 88.55)	Wilson score
Positive predictive value	52.24%	(40.48, 63.75)	Wilson score
Negative predictive value	89.01%	(83.78, 92.7)	Wilson score
Diagnostic accuracy	79.46%	(74.11, 83.94)	Wilson score

For the above observation as per Pearson chi square test, procalcitonin is highly significant in detecting bacterial infection, $p < 0.0001$.

The sensitivity and specificity of this test 62.5% and 84.16% according to Wilson's test within 95% confidence interval. The positive predictive value, which rules in an infection, is 52.24% but the negative predictive value, which rules out an infection, is 89%.

Fig. 9

Serum procalcitonin and final diagnosis

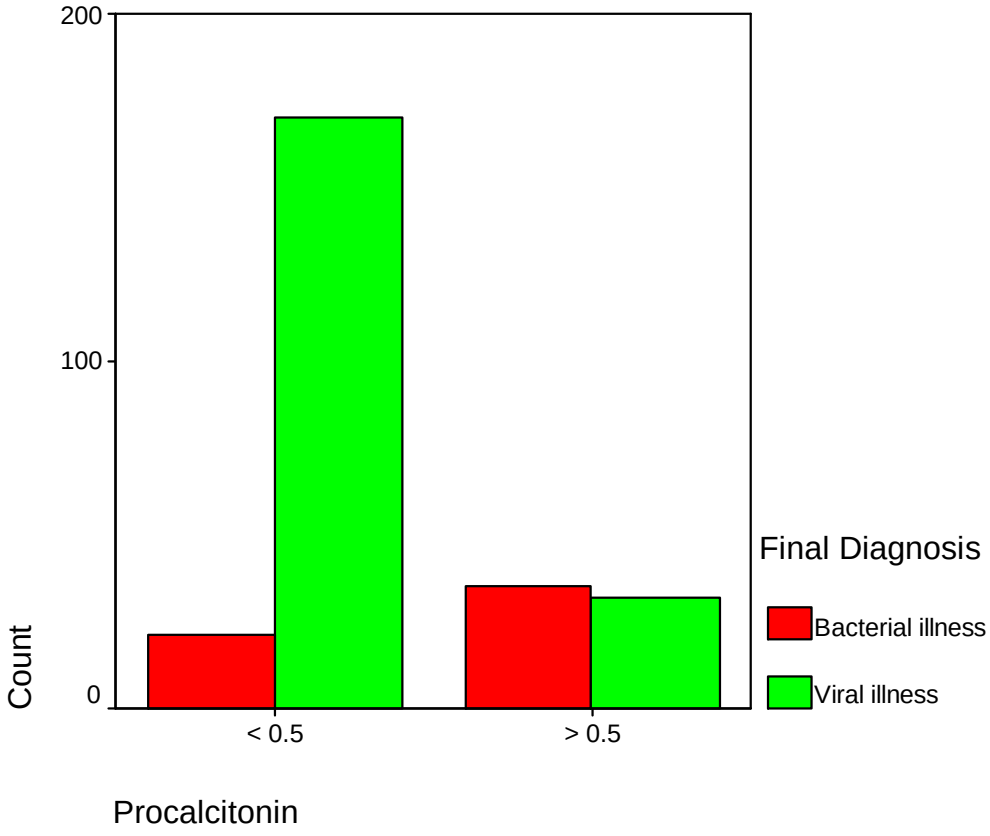


Table –14

Association between hs CRP and final diagnosis

	Final diagnosis			**Pearson chi-square value, df**	**P value**
hs CRPmg/L	Bacterial illness	Viral Illness	Total		
< =10	8 (14.3%)	77 (38.1%)	85(32.9%)	11.273(b), 1	<0.001**
> 10	48(85.7%)	125(61.9%)	173 (67.1%)		
Total	56 (100%)	202 (100%)	258 (100%)		

Of the 56 cases with bacterial infection, only 48 cases had CRP values of more than 10mg/l (85.7%) and the remaining 8 cases had CRP values of less than 10mg/l (14.3%). Of the total of 202 cases with viral infection, 125 cases had raised CRP values (61.9%) and the rest had CRP values less than 10mg/l. Thus CRP is very sensitive in detecting bacterial infections, with p value <0.001 which is highly significant.

Table – 15

Evaluation of hs CRP as a diagnostic test

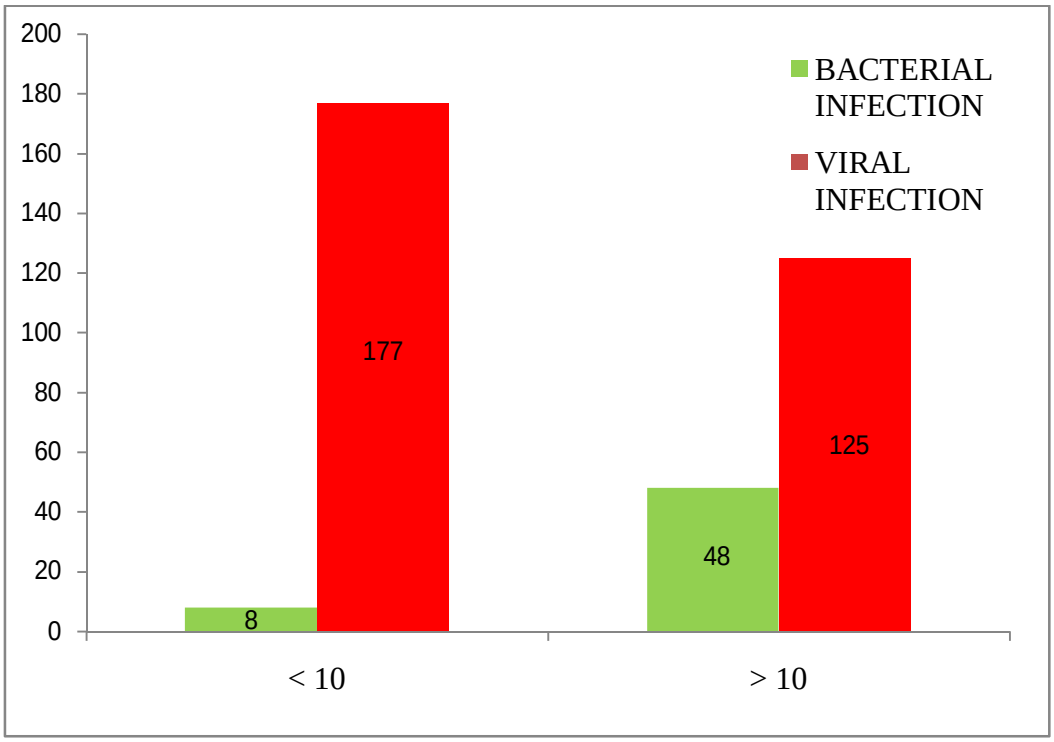
Parameter	Estimate	Lower - Upper 95% CIs	Method
Sensitivity	85.71%	(74.26, 92.58)	Wilson score
Specificity	38.12%	(31.7, 44.98)	Wilson score
Positive predictive value(PPV)	27.75%	(21.61, 34.85)	Wilson score
Negative predictive value (NPV)	90.59%	(82.51, 95.15)	Wilson score
Diagnostic accuracy	48.45%	(42.42, 54.53)	Wilson score

As per pearson-chi square test, the sensitivity of CRP in detecting bacterial infection is 85.71% and the cut off limit is 10mg/l and specificity is 38.12%

Positive predictive value is 27.75% and the negative predictive value is 90.59 % as per Wilson's method of analysis. The diagnostic accuracy of CRP in detecting bacterial infection is 48.45%.

Fig. 10

hs CRP and final diagnosis



177 children with CRP with <10mg/l had viral infection and 125 children with CRP >10 mg/l had viral infection.

Table 16

Association between absolute neutrophil count (ANC) and final diagnosis

ANC cells/mm^3	**Final Diagnosis**			**Pearson Chi-Square value, df**	**P value**
	Bacterial infection	**Viral infection**	**Total**		
< =5000	27(48.2%)	135 (66.8%)	162(62.8%)	6.504(b), 1	<0.011*
> 5000	29(51.8%)	67(33.2%)	96 (37.2%)		
Total	56 (100%)	202(100%)	258 (100%)		

Absolute neutrophil count is not a very sensitive or specific marker of bacterial infection in children because of age dependent variation in the leucocyte count in children. In our study, of the total of 258 children, 135 children (66.8%) who had viral infections had ANC of <5000 cells/mm$^{3.}$

Table 17

Association between absolute neurophil count (ANC) and Procalcitonin

ANC Cells/mm^3	**Procalcitonin ng/ml**		
	<=0.5	**>0.5**	**Total**
<=5000	132(69.1%)	30(44.8%)	162 (62.8%)
>5000	59 (30.9%)	37 (55.2%)	96(37.2%)
Total	191 (100.0%)	67 (100.0%)	258 (100.0%)

55.2% of the children with PCT >0.5ng/ml have ANC value of >5000 cells/mm^3 and 69.1% children with ANC <5000cells/mm ^{3} have PCT value of <0.5ng/ml

Table – 18

Evaluation of ANC as a diagnostic test

Parameter	Estimate	Lower - Upper 95% CIs	Method
Sensitivity	51.79%	(39.01, 64.33)	Wilson Score
Specificity	30.93%	(22.6, 40.7)	Wilson Score
Positive Predictive Value	30.21%	(21.93, 40.01)	Wilson Score
Negative Predictive Value	52.63%	(39.92, 65.01)	Wilson Score
Diagnostic Accuracy	38.56%	(31.22, 46.47)	Wilson Score

As per pearson-chi square test, the sensitivity of ANC in detecting bacterial infection is 51.79% and the specificity is 30.93%.

Positive predictive value is 30.21% only and the negative predictive value is 52.63% as per Wilson's method of analysis. The diagnostic accuracy of ANC in detecting bacterial infection is only 38.56%.

Table 19

Student t test and the group statistics between the variables, ANC & bacterial illness

	Final Diagnosis	N	Mean	Std. Deviation	Std. Error Mean
ANC	**Bacterial infection**	56	6135.3589	3549.38911	474.30707
	Viral infection	202	5017.3125	4096.87890	288.25539

As per the t – test, the mean value of ANC in cases with bacterial infection is >6000 cells/mm^3 and for viral illness ANC <6000 cells/mm^3

Table-20

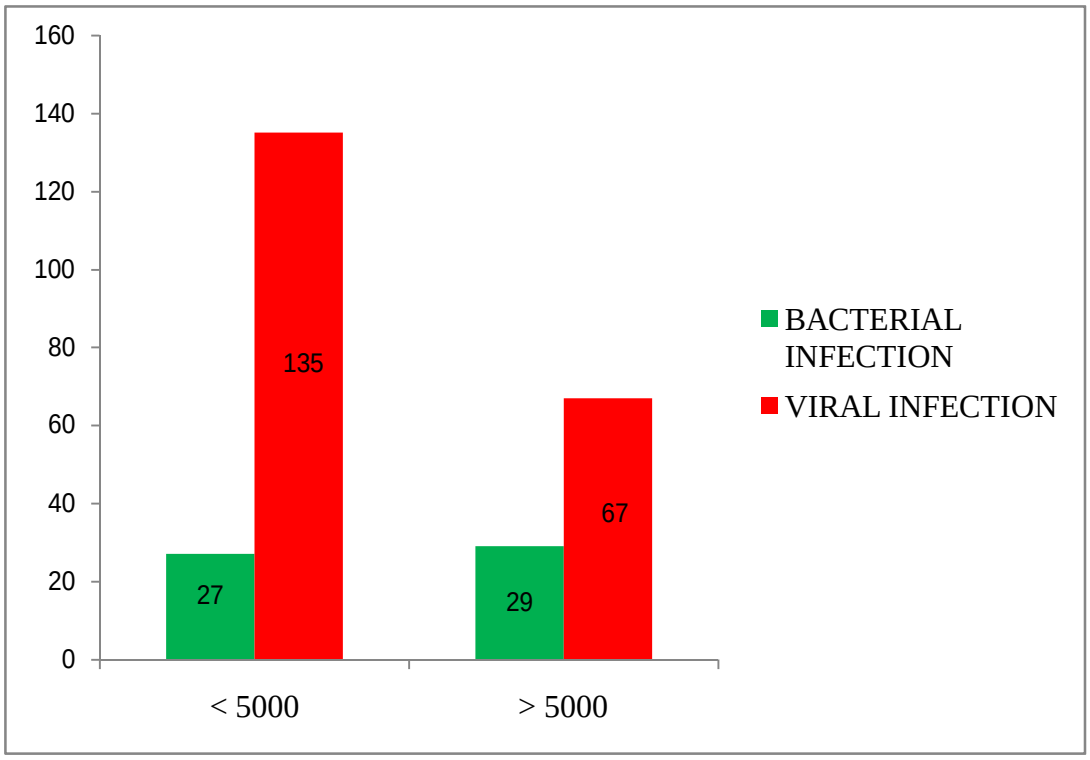
Student t test and the group statistics between the variables ANC & PCT

	Procalcito-nin ng/ml	**N**	**Mean**	**Std. Deviation**	**Std. Error Mean**
ANC	**< 0.5**	191	4853.6749	3895.01973	281.83374
	> 0.5	67	6418.2884	4114.69417	502.68990

As per the t–test, in the study population who had bacterial infection, the mean value of ANC is 6418 and in the same group with PCT <0.5ng/ml, the mean value of ANC is 4853.

Fig. 11

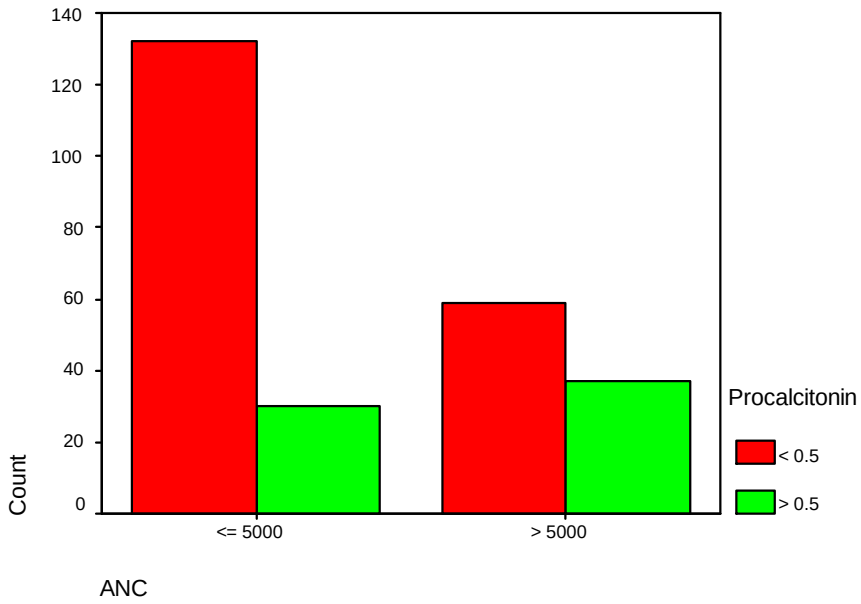
Absolute neutrophil count and final diagnosis



Proportion of bacterial infection with ANC <5000 cells/mm^3 is 48.2% and those with ANC>5000 cells/mm^3 is 33.2%

Fig. 12

Absolute neutrophil count and procalcitonin

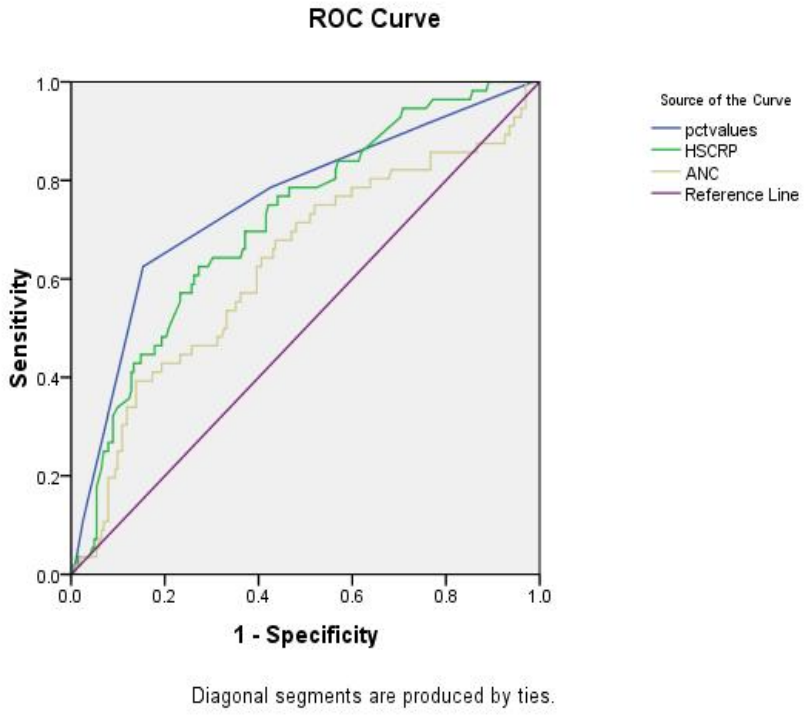


Significant proportion of children with ANC <5000 had bacterial infections and only few children with ANC>5000 had viral infections

Fig.13

Receiver operating characteristic (ROC) curve for

PCT, hs CRP & ANC



ROC curve for procalcitonin , ANC and HS CRP with respect to sensitivity and specificity.

Table – 21

Determination of area under curve (AUC) with ROC

Area Under the Curve (AUC)	
Test Result Variable(s)	**Area**
ANC	0.628
HS CRP	0.717
PCT	0.755

Procalcitonin has the greater AUC (0.755) as compared to hs CRP (0.717) and ANC (0.628)

Table 22

Comparison of characteristics of PCT, Hs CRP and ANC

Parameter	PCT	Hs CRP	ANC
Sensitivity	62.50%	**85.71%**	51.79%
Specificity	**84.16%**	38.12%	30.93%
PPV	**52.24%**	27.75%	30.21%
NPV	**89.01%**	**90.59%**	52.63%
Diagnosticaccuracy	**79.46%**	48.45%	38.56%
Odds ratio	**8.854**	3.696	0.4809

DISCUSSION

DISCUSSION

Children presenting to the outpatient department or being admitted as inpatients for fever is a very common problem in practice. Majority of these infections are viral in etiology and are easy to identify but a lesser proportion are bacterial requiring antibiotic therapy and more importantly, having the potential to evolve into serious infections like sepsis, meningitis etc. which can give rise to considerable morbidity and mortality.

This is particularly true for children less than 3 years of age in whom signs and symptoms may be subtle and can be missed by even the most experienced pediatrician. The need for coming to a diagnosis rapidly, coupled with the need for judicious use of antibiotics is a major challenge. A rapid diagnosis and treatment is important to reduce the progression to severe bacterial infections (SBI) which will result in poorer outcomes.

Also, the quicker the diagnosis is made the use of antibiotics can be justifiably reduced thereby reducing resistance and unnecessary costs of hospitalization can be avoided. So, the major aim in evaluating febrile children is – is this infection bacterial or not and can it progress to an SBI?

Much research has gone into finding the ideal marker that will pinpoint bacterial infections from amidst many viral infections. The ideal marker would be one with very high sensitivity and specificity, one which should rise very rapidly after the onset of the infection and most of all, should be easily available and not too expensive.

From amongst the various bio markers PCT, hs CRP and ANC have been studied rather frequently with varying reports on their reliability in predicting bacterial infections. This study was designed to compare these three parameters among febrile children, presenting to the OP/ IP, as to their accuracy in predicting bacterial infections.

The study population comprised of children who satisfied the inclusion criteria. Immediately after admission and diagnosis, blood samples were drawn for appropriate investigations, and based on the investigations, a final diagnosis was made and categorized into bacterial or viral infection. Treatment was initiated as per standard departmental protocol. PCT, hs CRP, ANC values were compared with the final diagnosis with regard to accuracy in diagnosing bacterial infections.

Procalcitonin:

Age related differences in the rise of procalcitonin value were studied (Table2).Very young children do not show any localising signs even in serious infectious conditions and in these situations biomarkers are used to aid the diagnosis. Procalcitonin values are not related to difference in age.

On comparing the efficacy of procalcitonin with the different age groups, it was found that procalcitonin is not an effective tool in the differentiation of bacterial illness from viral illness in children based on the age alone. Children in both the age groups showed a similar increase in procalcitonin while having a bacterial illness.

One clinical observation which deserves special mention is that children who are very young and present with shock during an acute febrile illness, have a significant increase in procalcitonin values above 2 ng/ml.

Quantitative measurement of procalcitonin can be of much use in estimating the severity of infection in such a sick child. In a meta analysis by Yo et al, eight studies were analysed which contained children < 36 months. They got a mean sensitivity of 83% and specificity of 89% for procalcitonin. This is in accordance with our study, the overall sensitivity being 62.5% and the specificity 84.1%.

Sex distribution:

The male: female ratio was approximately 1.4:1 (Fig. 7) There are no sex related variations in the distribution of procalcitonin values described in literature. Our study also did not show any relationship of PCT with reference to gender (Table 3).

Majority of the children admitted to our hospital had viral infections, 202 cases of the total 258 cases. The remaining 56 children had bacterial infection namely enteric fever, urinary tract infection (both of which had definite bacterial isolates on culture) and pneumonia and ASOM, which are mostly due to bacterial infection in children. The ratio of bacterial to viral illnesses was approximately 1:3 in our study population. Among the bacterial infections in our study, we had a higher proportion of enteric fever (35 cases), followed by urinary tract infection (10 cases).

Coming to the main study characteristic, serum procalcitonin level was >0.5ng/ml in 62.5% of children with bacterial infections, whereas only 15.8% of children who were diagnosed to have a viral infection had a PCT >0.5ng/ml. 84.2% of the children who had a PCT<0.5ng/ml were diagnosed to have a viral illness. Thus it can be inferred that the true positive values of PCT are more in case of bacterial infections. Hence, PCT has good predictive value for bacterial infection. As per the pearson chi square test, this is statistically significant with P <0.0001*(Table –

11). This result is similar to the results obtained by Simon et al and the meta analysis by Yo et al, which showed a similar significance of $P<0.05$.

The sensitivity of procalcitonin in detecting bacterial infections at a cut off of >0.5ng/ml comes to 62.5% and the specificity is 84.1%. These results are correlating with the results obtained by Andreola et al[56]. In their prospective, observational study done in 2007, in a pediatric unit, they enrolled 408 cases and evaluated the role of PCT, hs CRP and ANC in diagnosing bacterial infections in the age group <36 months. The sensitivity obtained in their study was 87.5% and specificity was 50%.

In our study, with the above sensitivity and specificity the positive predictive value of PCT is 52.4% and the negative predictive value is 89.01%. The diagnostic odds ratio for PCT is 8.854 (4.577 – 17.13).The positive likelihood ratio of PCT in predicting bacterial illness is 3.945 - (3.588 – 4.338) and negative likelihood ratio is 0.4456 (0.405 – 0.4902). This is similar to the results of Andreola et al and other studies.

Lacour et al[57], in their study in 2008, achieved a positive likelihood ratio of 4.92 (95% CI 3.26 – 7.43) and a negative likelihood ratio of 0.07 (0.02 – 0.27). They used a triad of urine dipstick testing along with hs CRP and PCT. The study by Thayyil et al[58] in 2005, reported the highest positive likelihood ratio of 10.67 (95% CI 2.9 – 39.3).

They had used thresholds for all the three blood tests i.e. procalcitonin > 2 ng/ml, hs CRP > 50 mg/l, and a WBC count of >15 X 10^9/l. The major drawback of this study was the negative likelihood ratio of 0.52 (0.25 – 1.05) which lacked 'rule out' value. That is this triad of cut off values could accurately 'rule in' but not 'rule out' bacterial infections.

Two studies have looked at the predictive value of hs CRP and PCT in febrile children less than 16 years of age, similar to our study. The largest one was by Gendrel et al, wherein PCT values were ascertained for 700 children and in about 360 patients an infectious etiology was obtained.

Children were assigned to three groups based on the final diagnosis – invasive bacterial infections (n=46), localized bacterial infections (n=78) and viral infections (n=236). The mean PCT level of the first group was 45.9 ng/ ml, the second was 4.2 ng/ ml and the third was 0.4 ng/ ml. PCT was found to be the most useful test, the next best being hs CRP.

Our study has remarkable similarities with the one done by Gendrel in that we too recruited all children less than 12 years of age, our proportions of children with bacterial and viral infections were about the same, PCT performed much better than hs CRP as a diagnostic tool to rule out bacterial infections and lastly, all patients were hospitalized.

Putto et al[59] studied hs CRP and WBC counts in 151 children and reported that hs CRP had a far superior sensitivity (100%) and specificity (75%) for the detection of bacterial infection and that WBC counts were far less sensitive and specific.

Thus, PCT has a diagnostic accuracy of 79.46%, in our study, in predicting bacterial infections in febrile children. Hence PCT is the best marker in reasonably excluding bacterial infection if the values are <0.5. Also, procalcitonin has a higher negative predictive value (89%) than positive predictive value (52.2%), in our study, hence it can be used for excluding or 'rule out' serious bacterial infections in children.

Further, on comparing the characteristics of culture proven bacterial infection with procalcitonin values, the following could be inferred. Of the total of 31 cases with blood culture positive, 19 cases (61.3%) had PCT values >0.5ng/dl. On the other hand, 227 cases with sterile blood culture, 179 cases (93.7%) had PCT values <0.5ng/ml. Thus, this supported our observation that PCT can be safely used in the exclusion of septicemia. The association is statistically significant with $p<0.05$ as per pearson chi square test.

Among the loco-regional infections studied, namely, urinary tract infections (UTI) in our case, it was found that PCT had a significant predictive value in diagnosing UTI. Literature search shows that the rise of PCT can be used in predicting upper urinary tract involvement.

In a study by Leroy et al[60] in 2011, PCT was found to demonstrate a reasonable diagnostic accuracy for both acute pyelonephritis and renal scarring and was a more accurate predictor than either hs CRP or WBC count. 99.5% cases with negative urine culture had PCT values <0.5ng/ml and only one case with positive urine culture had PCT <0.5 where as 88.9% cases with urine culture positivity had PCT values >0.5.

The rise of PCT correlates well with urinary tract infection with or without upper urinary tract involvement. Our study contained only cases with lower urinary tract involvement. Hence, it can be concluded that, UTI can be almost excluded if PCT <0.5ng/ml. The Pearson chi square correlation test for PCT in diagnosing UTI is highly significant with $P<0.0001^{*}$.

Yidiz et al studied hs CRP as a marker of renal scarring. They found that the rise of CRP can be correlated with renal scarring. Xu et al investigated the role of PCT in diagnosing UTI and found that PCT has a role in predicting pyelonephritis better than with hs CRP.

They noted that the average PCT and CRP levels were much higher in children with acute pyelonephritis than in those with lower UTIs ($p<0.01$) while white cell counts were not useful in predicting renal involvement. The areas under the PCT, CRP and, WBC curves were 0.958, 0.858 and 0.588 respectively.

Since there is no existing literature regarding varying combinations of clinical data and the procalcitonin values, an attempt was made in our study for the same. We attempted to study the association between total duration of fever in days and the rise of serum procalcitonin levels.

Statistical analysis showed that the association between the two was not significant but suggestive. That is children who present to us with more than 7 days of fever have a high likelihood of evolving into a bacterial infection. This is also supported by the fact that most self limiting viral illness in pediatric age group lasts for not more than a week. The statistical association between the total number of days of fever at presentation to the rise of procalcitonin was weak in our study with a P >0.05.

Further, procalcitonin values were analysed with the day of clinical defervescence of fever to see whether initial levels of PCT correlated with defervescence of fever. Of the total of 258 cases, 236 cases had fever defervescence in less than 5 days (91.5%). Of the total, 8.5% children had fever defervescence after 5 days, 12 cases had serum procalcitonin values <0.5ng/ml and 10 cases had >0.5ng/ml.

This association was statistically significant with P <0.05. The inference being, higher the rise of procalcitonin, higher the possibility of bacterial infection and more is the time taken for fever defervescence. At the time of writing, a study conducted by the National Institutes of

Health, looking at this association has been completed. The results of this study are yet to be made public.

Hs CRP:

The second parameter studied was hs CRP. Hs CRP had a cut off level of 10 ng/ ml in our study for the presumptive diagnosis of bacterial infection. This low value was taken as cut off because the kit used in our study has a very high sensitivity of detecting values as low as 0.2 ng/ml. With this cut off, of the total 173 children with values more than 10, 48 had bacterial illness and 125 cases had viral illness.

This can be interpreted as 85.7% of the children with bacterial illness and 61.9% of the children had viral illness had CRP value of >10mg/L. Only 14.3% (8 cases) had hs CRP values of < 10mg/L, were diagnosed to have a bacterial infection. This has statistical significance of $P<0.001$ with pearson chi square test.

The sensitivity of hs CRP in detecting bacterial infection is 85.71% and specificity is 38.12%. The low specificity of CRP in our study can be because of the lesser cut off of CRP used for the diagnosis and the fact that CRP was evaluated early in the course of the disease well before the CRP values actually started to peak.

In a meta analysis by Yo et al, in studying the test characteristics of procalcitonin and CRP in detecting possible serious bacterial infection,

they reviewed a study done by Olaciregui et al[61], in 2009. It was a prospective observational study. They used a higher cut off level of CRP of 30 ng/ ml with a prevalence of serious bacterial infection of 23.63%. They obtained a sensitivity of 63.4% and a specificity of 84.2%.Yo et al found the mean AOC for CRP to be 0.84, which is correlating with our study in which the AOC for CRP is 0.717.

The positive predictive value of CRP in our study is 27.75% which is less than that for procalcitonin. The negative predictive value of CRP is high 90.59% and is comparable to that of procalcitonin i.e. 89%.

Thus, it can be concluded that CRP is inferior to procalcitonin in diagnosing or 'ruling in' bacterial infection. The positive likelihood ratio of CRP is 1.385 (1.354 – 1.417) and the negative likelihood ratio is 0.374 (0.2815 – 0.499) which are inferior to those obtained with procalcitonin. The diagnostic odds ratio comes around 3.696 for CRP.

ANC:

Moving on to the third marker in our study, namely, absolute neutrophil count, statistical analysis shows that it does not correlate well with bacterial infections. Based on group statistics, the mean value of ANC in the cases with bacterial illness is 6135 cells a standard deviation of 3549 cells and a standard error of 474 cells..

Similarly in the study group with PCT >0.5ng/ml, the mean ANC is 6418 cells. Thus bacterial infection can be suspected if ANC is approximately >6000cells/mm^3. It is also seen that the mean ANC if the PCT values are <0.5ng/ml is 4853 cells. Of the total 96 children with ANC >5000, only 29 had bacterial illness and the remaining 67 had viral illnesses. Thus to conclude, bacterial infection can be predicted if PCT >0.5ng/ml and ANC is more than 6000 cells/mm^3.

ANC alone is not a reliable indicator in diagnosing bacterial infection. In our study, the sensitivity of ANC in detecting bacterial infection is 51.79% and the specificity is 30.93%. Thus, ANC is inferior to both PCT and hs CRP in detecting bacterial infection in febrile children.

The positive predictive value of ANC is 30.21% and the negative predictive value is 52.63% with a diagnostic accuracy of 38.56%. This is in accordance with the study conducted by Thayyil et al[58] in 2005 using leucocyte count. They found a sensitivity of 50 % and a specificity of 53.1% in diagnosing bacterial infection. In our study, the positive likelihood ratio of ANC in detecting bacterial infection is 0.7497(0.6837 - 0.8221) and a negative likelihood ratio is 1.559(1.253 - 1.94) which is third after PCT and hs CRP. The diagnostic accuracy of ANC is thus 38.56% which is much less than that for PCT and CRP.

This was further supported by the area under the curve being the least for ANC (0.628) which makes it a poor test. These findings are similar to those reported by Andreola et al.

The accuracy of the diagnostic test is to be evaluated with the positive predictive value of that test and the area under curve given by the receiver operating characteristic curve. The positive predictive value of procalcitonin is higher compared to hs CRP and absolute neutrophil count in predicting bacterial infection. Thus procalcitonin when used in isolation can be relied upon to diagnose bacterial infection. This is in accordance with several studies available in literature.

CRP at a cut off of 10 mg/l is inferior to procalcitonin in detecting bacterial infection in our study though it is statistically significant. The results of hs CRP have to be interpreted in accordance with the clinical condition of the patient. ANC cannot be reliably used in the diagnosis of bacterial infection in isolation.

Likewise, among all the three parameters, PCT has the highest AUC (0.755) followed by CRP (AUC 0.717) and ANC (AUC 0.628). This is in accordance with the review study conducted by Yo et al in which PCT had the highest AUC compared to CRP and total leucocyte count.

To conclude, among ANC, hs CRP and procalcitonin, procalcitonin emerges as the single best diagnostic marker in identifying bacterial infection in febrile children. Procalcitonin is a more specific rather than a sensitive marker in diagnosing bacterial illness. Thus PCT can be used to

exclude possible serious bacterial infection when the values are <0.5ng/dl and when used as a single parameter.

In the emergency department, either PCT can be used either singly or in combination with hs CRP in diagnosing bacterial infection. Having said that, it has to be kept in mind that, since the costs associated with missing serious bacterial infection is high, we recommend that procalcitonin should not be used in isolation. It is always better to use it along with other biomarkers. Many clinical trials have shown better advantages in term of patient improvement and cost reduction i.e. showing a high cost benefit ratio when procalcitonin was used in the management algorithm.

From our study, based on the above statistical analysis, we could suggest the following parameters pointing towards bacterial infection:

1) Fever >7 days
2) Procalcitonin >0.5ng/ml
3) Hs crp >10mg/L
4) Absolute neutrophil count >6000cells/cumm
5) Total days of fever defervescence >5 days

Thus in future, a clinical score can be evolved with much larger studies predicting the possibility of bacterial infection

In summary, our study showed that PCT performs better than hs CRP in detecting bacterial infection. Considering the fact that the sensitivity is rather poor and specificity is acceptable, values <0.5ng/ml can reasonably used for ruling excluding bacterial infection. However, PCT values >0.5ng/ml are not confirmatory evidence of a bacterial infection.

At this point, the available literature does not show how to combine procalcitonin with clinical data to improve the overall diagnostic performance. Larger studies are essential in children with accurate study design for the same .

CONCLUSION

CONCLUSION

- Procalcitonin may be useful, as a single test, in identifying bacterial infections in febrile children.

- Bacterial infections may be reasonably excluded if PCT values are <0.5ng/ml

- Hs - CRP is comparable with PCT in identifying bacterial infection

- ANC is less useful in identifying bacterial infection.

LIMITATIONS

LIMITATIONS

- The kit used for measuring serum procalcitonin is a semi quantitative method. Hence absolute values of PCT were not estimated.
- Multiple i.e. serial estimations of the inflammatory markers were not done. Serial procalcitonin measures will not only indicate improvement, but will also limit the duration of unnecessary antibiotic therapy.
- More than 60% of the children enrolled in this study were diagnosed to have viral infection. Hence procalcitonin values were better for ruling out bacterial infection.
- The cut off values for CRP is taken as 10 mg/L which were less compared to literature previously studied.

RECOMMENDATIONS

RECOMMENDATIONS

- In children presenting with fever, at all age groups, procalcitonin along with hs-CRP may be used as a rapid screening test to ascertain the likelihood of bacterial infections.

- A well designed study correlating clinical and vital signs along with testing for hs-CRP and PCT needs to be carried out from which a risk prediction score can be evolved.

- Further studies to ascertain different cut off values for PCT are needed – one which will decide the start of antibiotic therapy and another that will determine the discontinuation of treatment.

REFERANCES

1. Craig JC, Williams GJ, Jones M, Codarini M, Macaskill P, Hayen A et al. The accuracy of clinical symptoms and signs for the diagnosis of serious bacterial infection in young febrile Children: prospective cohort study of 15 781 febrile illnesses. BMJ 2010; 340:c1594.

2. Van den Bruel A, Thompson MJ, Haj-Hassan T, Steven R, Moll H, Lakhanpur M, Mant D. Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review. BMJ 2011; 342:d3082 doi:10.1136/bmj.d3082.

3. Ginocchio CC. Strengths and Weaknesses of FDA-Approved/ Cleared Diagnostic Devices for the Molecular Detection of Respiratory Pathogens. Clinical Infectious Diseases 2011; 52(S4):S312–S325

4. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. Cochrane Database of Systematic Reviews 2005; Issue 4. Art. No.: CD003539. DOI: 10.1002/14651858.CD003539.pub2.

5. Lever A, Mackenzie I Clinical review. Sepsis: definition, epidemiology and diagnosis. BMJ 2007; 335:879-83.

6. De S, Williams GJ, Hayen A, Macaskill P, Mccaskill M, Isaacs D et al. Accuracy of the “traffic light” clinical decision rule for serious bacterial infections in young children with fever: a retrospective cohort study. BMJ 2013; 346:f866

7. Arkader R, Troster EJ, Lopes MR, Junior RR, Carcillo JA, Leone C et al. Procalcitonin does discriminate between sepsis and systemic inflammatory response syndrome. Arch Dis Child 2006; 91:117–120.

8. Nelson GE, Mave V, Gupta A. Biomarkers for Sepsis: A Review with Special Attention to India. Biomed Research International Volume 2014, Article ID 264351.

9. Mona Nabulsi, Hani M, Karam M. Impact of C-reactive protein test results on evidence-based decision-making in cases of bacterial infection. BMC Pediatrics 2012; 12:140

10. Kaya Z , Küçükcongar A, Vurallı D, Emeksiz HC et al.Leukocyte Populations and C - reactive protein as Predictors of Bacterial Infections in Febrile Outpatient Children. Turk J Hematol 2014; 31:49-55

11. Stephen W, Standage1, Wong HR. Biomarkers for pediatric sepsis and septic shock. Expert Rev Anti Infect Ther. 2011 January; 9(1): 71–79.

12. Raghunath D. Emerging antibiotic resistance in bacteria with special reference to India J. Biosci 33: 593–603

13. Simon L, France Gauvin F,Devendra K. Amre D,Patrick Saint-Louis Pet al. Serum Procalcitonin and C - reactive protein Levels as Markers of Bacterial Infection: A Systematic Review and Meta-analysis. Clinical Infectious Diseases 2004; 39:206–17.

14. Adib M, Zahra ,Bakhshiani Z ,Fakhri Navaei F , Fouladi S, Procalcitonin: A Reliable Marker for the Diagnosis of Neonatal Sepsis. Iran J Basic Med Sci. 2012 Mar-Apr; 15(2): 777–782.

15. Korppi M, Remes S,. Serum procalcitonin in pneumococcal pneumonia in children. Eur Respir J 2001; 17:623-7

16. Olaciregui EI, Hernandez U, Munoz JA, et al. Markers that predict serious bacterial infection in infants under 3 months of

age presenting with fever of unknown origin. Arch Dis Child. 2009;94(7):501–5

17. Future Research Needs on Procalcitonin- Guided Antibiotic Therapy. AHRQ Publication No.13-EHC034-EF :January 2013

18. Giamarllos Bourboulis EJ, Mega, Grecka P, et al. Procalcitonin: a marker to clearly differentiate systemic inflammatory response syndrome and sepsis in the critically ill patient? Intensive Care Med 2002; 28:1351-6.

19. I Delèvaux, M André, M Colombier, E Albuisson et al. Can procalcitonin measurement help in differentiating Between bacterial infection and other kinds of inflammatory processes? Ann Rheum Dis 2003; 62:337–340

20. Hatherill M, Tibby SM, Sykes K, Turner C, Murdoch IA., Diagnostic markers of infection: comparison of procalcitonin with C reactive protein and leucocyte count. Arch Dis Child 1999; 81:417–421

21. Ibrahim KA, Abdel-Wahab AA, Ibrahim AS. Diagnostic value of Serum Procalcitonin Levels in children with meningitis: a comparison with blood leukocyte count and C-reactive protein. J Pak Med Assoc; Vol. 61, No. 4, April 2011

22. Van den Bruel A, Thompson MJ, Haj-Hassan T, Stevens R et al. Diagnostic value of laboratory tests in identifying serious infections in febrile children: systematic review. BMJ 2011 Jun 8; 342:d3082. Doi: 10.1136/bmj.d3082

23. Abaci1A, Öktem MA, Ünal E, Türkmen MA. Utility of the Serum C - reactive protein and Procalcitonin for Detection of Occult Bacterial Infection In 3-36 Month Old Children. Journal of Ankara University Faculty of Medicine 2008; 61(2)

24. Schutz P. Using procalcitonin- guided algorithms to improve antimicrobial therapy in ICU patients with respiratory infections and sepsis.. Curr Crit Care2013 Oct; 19(5):453-6

25. M,Michael Goldman M,Kozer E.Extreme leucocytosis and the risk of serious bacterial infections in febrile children.*Arch Dis Child 2010;95:209-212*

26. Assicot M , Gendrel O, Raymond J et al,Measurement of procalcitonin levels in children with bacterial or viral meningitis. Clin Infect Dis 1997; 24:1240-2.

27. Dandona P, Nix D, Wilson MF, Aljada A et al. Procalcitonin increase after endotoxin injection in normal subjects. J Cin Endocrinol Metab 1994; 79:1605-8.

28. Tang BM, Eslick GD, Craig JC, mclean AS. Review: Accuracy of procalcitonin for sepsis diagnosis in critically ill patients: systematic review and meta-analysis: Vol 7: 2007

29. Jereb M, Muzlovic I, Hojker S, Strl F., et al. Predictive value of serum and cerebrospinal fluid procalcitonin levels for the diagnosis of bacterial meningitis. Infection 29, 209–212

30. Giamarellos-Bourboulis EJ, Mega A, Grecka P, Scarpa N, Koratzanis G, Thomopoulos G, Giamarellou H: **Procalcitonin: a marker to clearly differentiate systemic inflammatory responsesyndrome and sepsis in the critically ill patient?** ***I****ntensive Care Med* 2002, **28:**1351-1356.

31. O'connor E, Venkatesh B, Lipman J, Mashongonyika C, Hall J et al. Special reviews:Procalcitonin in Critical Illness. (criticalcare andresusitation 2001;3:236

32. Oberhofer D, Juras J , Žurić P, and Rumenjak V et al Comparison of C-reactive protein and procalcitonin as predictors of postoperative infectious complications after elective colorectal surgery Croat Med J. 2012;53:612-9

33. Yukioka H, Aikawa N, Fujishima S, Kogawak et al. Multicenter prospective study of procalcitonin as an indicator of sepsis original article. J Infect Chemother (2005) 11:152–159

34. Herd D. In children under age three does procalcitonin help exclude serious bacterial infection in fever without focus? Archimedes doi: 10.1136/adc.2006.112441

35. Dauber et al. Procalcitonin in young febrile infants for the detection of serious bacterial infections. Pediatrics 2008; 122:701–710.

36. Maniaci V, Dauber A, Weiss S, et al. Procalcitonin in young febrile infants for the detection of seious bacterial infections. Pediatrics 2008; 122:701–710.

37. Baer G, Baumann P, Buettcher M, Heininger U et al. Procalcitonin Guidance to Reduce Antibiotic Treatment of Lower Respiratory Tract Infection in Children and Adolescents (propaed): A Randomized Controlled Trial. Plos One 8(8): e68419. Doi:10.1371/journal.pone.006841947)

38. Schutz P. Using procalcitonin- guided algorithms to improve antimicrobial therapy in ICU patients with respiratory infections and sepsis.. Curr Crit Care2013 Oct; 19(5):453-6

39. Angus D C, Huang D T, Weissfeld LA , Kellum K A, et al. Risk prediction with procalcitonin and clinical rules in community-acquired pneumonia. Ann Emerg Med. Jul 2008; 52(1): 48–58.e2.

40. Gendrel, Dominique , Raymond, Josette coste, Joel; moulin, Florence et al; Comparison of procalcitonin with C-reactive protein, interleukin 6 and interferon-alpha for differentiation of bacterial vs. Viral infections Pediatric Infectious Disease Journal: October 1999 - Volume 18 - Issue 10 - pp 875-881

41. Brauner M,Michael Goldman M,Kozer E.Extreme leucocytosis and the risk of serious bacterial infections in febrile children.*Arch Dis Child* 2010;95:209-212

42. Ayazi P, Mahyar M,Hashemi HJ,Mahdi M Karimzadeh Te Comparison of Procalcitonin and C Reactive Protein Tests in Children with Urinary tract infection Iran J Pediatr Dec 2009; Vol 19 (No 4), Pp:381-386

43. **Xu** R, **Liu H**, **Liu J**, **Dong** J et al in 2014 Procalcitonin and C-reactive protein in urinary tract infection diagnosis BMC Urology 2014, 14:45 doi: 10.1186/1471-2490-14-45

44. Al-Majali RM. White blood cell count, absolute neutrophil count, as predictors of hidden Bacterial infections in febrile children 1-18 months of age without focus. Pak J Med Sci April-June 2004; Vol: 20 No. 2: 97-100

45. Saskia F et al. Use or serum CRP and procalcitonin in addition to symptoms and signs to predict pneumonia presenting to primary care with acute cough-diagnostic study. Bio Med Research International Volume 2014 (2014), Article ID 264351, 11 pages.

46. Moulin F, Raymond J, Lorrot M, Marc E, Coste J, Iniguez JL et al. Procalcitonin in children admitted to hospital with community acquired pneumonia. Arch Dis Child 2001; 84:332–336

47. Yo , Hsieh PS, Lee SH, Wu JY et al Comparison of the Test Characteristics of Procalcitonin to C-Reactive Protein and

Leukocytosis for the Detection of Serious Bacterial Infections in Children Presenting With Fever Without Source: A Systematic Review and Meta-analysis. Annals of Emergency Medicine Volume Volume 60.

48. Nabulsi M, Hani M, Karam M. Impact of C-reactive protein test results on evidence-based decision-making in cases of bacterial infection. BMC Pediatrics 2012; 12:140

49. Oosterheert J J, Bruns A H W, Hak E and Hoepelman. Usefulness of consecutive C reactive protein in the severity of community acquired pneumonia

50. Mannan A, Shohel M, Rajia S, Mahmud N et al.Cross sectional study on antibiotic resistance pattern of Salmonella typh*i* clinical isolates from Bangladesh. Asian Pac J Trop Biomed. Apr 2014; 4(4): 306–311. Doi: 10.12980/APJTB.4.2014C770

51. Finch R. Bacterial resistance—the clinical challenge. Clinical Microbiology and Infection, 2002; Volume 8: Supplement 3

52. Kotwani A and Holloway K. Trends in antibiotic use among outpatients in New Delhi, India. BMC Infectious Diseases 2011, 11:99

53. Alvarez-uria G, Zachariah S, Thomas D. High prescription of antimicrobials in a rural district hospital in India. Pharmacy Practice 2014 Apr-Jun; 12(2):384.

54. Finch R, Hunter PA. Antibiotic resistance—action to promote new technologies:Report of an EU Intergovernmental Conference held in Birmingham, UK, 12–13 December 2005.Journal of Antimicrobial Chemotherapy; 2006:58

55. Oosterheert J, Anton M, Schuurman R, Andy I. M, Hoepelman Hak E. Impact of Rapid Detection of Viral and Atypical Bacterial Pathogens by Real-Time Polymerase Chain Reaction for Patients

with Lower Respiratory Tract Infection. Clinical Infectious Diseases 2005; 41:1438–44.

56. Andreola B, Bressan S,Callegaro S, Liverani A, Plebani M, and Dalt L et al. Procalcitonin and C-Reactive Protein as Diagnostic MarkersOf Severe Bacterial Infections in Febrile Infants and ChildrenIn the Emergency Department. Pediatr Infect Dis J2007;26: 672–677

57. Lacour, Zamora S, Gervaix A, . Bedside Procalcitonin and C-Reactive Protein Tests in Children With Fever Without Localizing Signs of Infection Seen in a Referral Center *Pediatrics Vol. 112 No. 5 2003 pp. 1054 -1060 (doi: 10.1542/peds.112.5.1054)*

58. Thayyil S, Shenoy M,Hamaluba M,Gupta A, Frater J and Verber I. Is procalcitonin useful in early diagnosis of serious bacterial infections in children?. Acta paediatricavolume 94, Issue 2, pages 155–158, February 2005

59. Putto A, Ruuskanen O, Meurman O, et al. C-reactive protein in the evaluation of febrile illness.Arch Dis Child1986;61:24–29

60 Leroy S and Gervaix A. Procalcitonin: A Key Marker in Children with Urinary Tract Infection. Adv Urol. 2011; 2011: 397618.

61. Olaciregui I, Hernandez J, Munoz J A, Emparanza I, Landa JJ.Markers that predict serious bacterial infection in young infants presenting with fever of unknown origin. Arch.dis.child 94:2009,501-505

PROFORMA

SAMPLE NO

- Name DOA- IP no-
- Age DOD-
- Sex
- Informant Provisional diagnosis-
- Reliability
- Address
- Presenting complaints with duration:
- h/o Fever -
- h/o Cough & cold-
- h/o Vomiting-
- h/o Loose stools-
- h/o Abdominal pain –
- h/o Myalgia-

- h/o Burning micturition –
- h/o Seizures-
- h/o Yellowish discoluration of eyes, urine-
- Past h/o:
- Family h/0 – connective tissue disorders:
- Drug h/o-

Examination

- Vital signs-
- General examination-
- Systemic examination-

  CVS-

  RS-

  ABDOMEN-

  CNS

Investigations :

- Total count & Differential count

- Peripheral smear study
- Hs CRP
- Serum Procalcitonin level
- Defervesence of fever
- LFT
- Blood culture
- Urine culture
- CXR
- Final diagnosis
- Treatment

PATIENT CONSENT FORM

Study title:

SERUM PROCALCITONIN AS A DIAGNOSTIC MARKER OF BACTERIAL INFECTION IN FEBRILE CHILDREN

Study centre: ESI-PGIMSR, K.K.Nagar, Chennai

Participant name: Age: Sex:

I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to clarify all my queries and doubts and they have been answered to my satisfaction.

Investigator explained very well about the procedure and I am made aware of the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is purely voluntary and that I am free to withdraw at anytime without giving any reason.

I have understood that the investigator, regulatory authorities and the ethics committee will have access to my health records both in respect to current study and any further research that may be conducted in relation to it, even if I decide to withdraw from the study. I have understood that my identity will not be revealed in anyway and information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Without any compulsion I am willing to give consent for the participation of my child in this study.

Date: Signature / thumb impression of patient

Place:

Patient name:

Signature of the investigator:

Name of the investigator:

Sl.No	Age in years	Age	sex	Fever	TLC	Neutrophils	ANC	HS CRP	Procalcitonin	blood C/S	Urine c/s	Defervescence	final diagnosis		
1	sabari	4	Male	4	5900	36	2124	10	< 0.5	Positive	Negative	2	Bacterial illness		
2	harish	2	Male	5	24000	57	13680	10	< 0.5	Negative	Negative	6	Viral illness		
3	dharsini	6	Female	5	4000	49.4	1976	2	< 0.5	Negative	Negative	2	Viral illness		
4	mathiyarasan	1	Male	4	10000	42.1	4210	10	< 0.5	Negative	Negative	2	Viral illness		
5	madhesh	2	Male	4	6100	58.7	3580.7	49.5	< 0.5	Positive	Negative	3	Bacterial illness		
6	tharun	3	Male	10	8500	27.2	2312	12.2	< 0.5	Negative	Negative	3	Viral illness		
7	prakash kumar	12	Male	3	10200	56.4	5752.8	147.1	< 0.5	Negative	Negative	3	Viral illness		
8	raghav	2	Male	4	13400	67.3	9018.2	17.2	< 0.5	Negative	Negative	3	Bacterial illness		
9	harikrishnan	7	Male	3	9400	71.2	6692.8	10	< 0.5	Positive	Negative	4	Bacterial illness		
10	srimathi	6	Female	9	18800	84.1	15810.8	89	< 0.5	Negative	Negative	2	Viral illness		
11	naveena	12	Female	2	9300	80	7440	4.8	< 0.5	Negative	Negative	2	Viral illness		
12	naveen kumar	10	Male	2	9100	74	6734	5.1	< 0.5	Negative	Negative	3	Viral illness		
13	mounica	10	Female	5	6700	47.4	3175.8	55.8	< 0.5	Positive	Negative	7	Bacterial illness		
14	sethupriya7	10	Female	9	5700	72.7	4143.9	119.2	0.5-2.0	Positive	Negative	5	Bacterial illness		
15	priya	10	Female	4	9700	32.6	3162.2	2.7	< 0.5	Negative	Negative	2	Viral illness		
16	manimegalai	3	Female	4	19500	70.9	13825.5	18.6	< 0.5	Negative	Negative	3	Viral illness		
17	boni	9	Male	7	6500	64.7	4205.5	48.5	0.5-2.0	Positive	Negative	6	Bacterial illness		
18	vaishnavi	10	Male	3	5300	49.4	2618.2	10	< 0.5	Negative	Negative	6	Viral illness		
19	julian immanuael rohith	6	Female	7	18700	88.5	16549.5	1.1	< 0.5	Negative	Negative	1	Viral illness		
20	nithish raj	1	Male	1	30000	58.1	17430	10.9	2.1-10	Negative	Negative	1	Viral illness		
21	sridevi	6	Female	6	4100	39.5	1619.5	61.3	0.5-2.0	Negative	Negative	1	Viral illness		
22	tamilarasi	11	Female	7	15900	65	10335	109.7	< 0.5	Negative	Negative	3	Viral illness		
23	pratap kumar	5	Male	10	30000	80.5	24150	116.7	< 0.5	Negative	Negative	5	Viral illness		
24	dharanidharan	6	Male	7	7000	68.6	4802	21.8	< 0.5	Positive	Negative	7	Bacterial illness		

25	rajesh kumar	11	Male	2	4800	54.7	2625.6	6.9	0.5-2.0	Negative	Negative	1	Viral illness		
26	bhuvaneswaran	5	Male	5	4000	19.6	784	1.7	2.1-10	Negative	Negative	1	Viral illness		
27	monica	1	Female	5	7900	46.4	3665.6	14.2	< 0.5	Negative	Negative	3	Viral illness		
28	kavinesh	4	Male	3	13000	47.3	6149	19.2	< 0.5	Negative	Negative	4	Viral illness		
29	vignesh	10	Male	7	12340	56.4	6959.76	15.3	< 0.5	Negative	Negative	3	Viral illness		
30	joanna maria	5	Female	3	6800	65.3	4440.4	56.3	2.1-10	Positive	Negative	6	Bacterial illness		
31	sai karthikeyan	1	Male	5	12200	73.4	8954.8	45.3	< 0.5	Negative	Negative	3	Viral illness		
32	muthukumar	2	Male	4	9800	60	5880	10	< 0.5	Negative	Negative	3	Viral illness		
33	malar	4	Female	5	5600	68.3	3824.8	23.3	0.5-2.0	Negative	Positive	5	Bacterial illness		
34	senthil murugan	6	Male	3	12000	34.3	4116	12.2	2.1-10	Negative	Negative	3	Viral illness		
35	sumathi b/o	1	Male	2	10200	43.3	4416.6	12	< 0.5	Negative	Negative	4	Viral illness		
36	preethi	6	Female	5	5600	65.3	3656.8	12.3	0.5-2.0	Negative	Negative	4	Viral illness		
37	mahalakshmi	9	Female	4	7800	45.6	3556.8	9.7	< 0.5	Negative	Negative	2	Viral illness		
38	akshaya	5	Female	1	10200	78.3	7986.6	34.3	0.5-2.0	Positive	Negative	6	Bacterial illness		
39	suganthi	3	Female	1	12000	45.2	5424	12.3	0.5-2.0	Negative	Negative	4	Viral illness		
40	subbulakshmi	3	Female	4	9800	45.1	4419.8	23.2	< 0.5	Negative	Negative	3	Viral illness		
41	mohanashri	1	Female	2	10200	54.8	5589.6	18	< 0.5	Negative	Negative	4	Viral illness		
42	sriman	3	Male	4	12300	23	2829	9.2	< 0.5	Negative	Negative	3	Viral illness		
43	sanjay	11	Male	2	10200	45.3	4620.6	11.5	< 0.5	Negative	Negative	4	Viral illness		
44	yaazhni	4	Female	1	6900	34.3	2366.7	9.8	< 0.5	Negative	Negative	3	Viral illness		
45	ancy jeshni	1	Female	5	10300	54.3	5592.9	10.2	2.1-10	Negative	Positive	2	Bacterial illness		
46	loganathan	10	Male	1	9800	23.2	2273.6	13.2	< 0.5	Negative	Negative	4	Viral illness		
47	sai raj	4	Male	4	9800	78.3	7673.4	16.4	< 0.5	Negative	Negative	4	Viral illness		
48	sriram	5	Male	3	10200	45.3	4620.6	20.1	< 0.5	Negative	Negative	5	Viral illness		
49	shyam	6	Male	3	5600	78.3	4384.8	56.3	2.1-10	Positive	Negative	5	Bacterial illness		
50	vikesh	4	Male	3	12890	23.2	2990.48	34.3	< 0.5	Negative	Negative	5	Viral illness		
51	kishore	5	Male	3	8900	45.4	4040.6	12.9	< 0.5	Negative	Negative	4	Viral illness		
52	sunil kumar	8	Male	2	11200	34.3	3841.6	34.2	< 0.5	Negative	Negative	4	Viral illness		

53	parameshwari	5	Male	2	7800	54.3	4235.4	10.8	< 0.5	Negative	Negative	3	Viral illness		
54	lakshanethra	1	Female	5	6900	23.2	1600.8	9.3	< 0.5	Negative	Negative	3	Viral illness		
55	yuvaraj	12	Male	3	8900	34.4	3061.6	23.2	< 0.5	Negative	Negative	3	Viral illness		
56	guruprasad	7	Male	1	7800	56.4	4399.2	18.3	< 0.5	Negative	Negative	4	Viral illness		
57	nithish raj	7	Male	4	11200	45.3	5073.6	19.2	< 0.5	Negative	Negative	2	Viral illness		
58	madhan	5	Male	3	12200	67.3	8210.6	67.4	< 0.5	Negative	Negative	4	Viral illness		
59	monisha	9	Female	2	5600	23.3	1304.8	23.2	< 0.5	Negative	Negative	7	Bacterial illness		
60	sabir basha	12	Male	7	13400	54.3	7276.2	13.3	< 0.5	Negative	Negative	4	Bacterial illness		
61	jothika	7	Female	3	10200	34.3	3498.6	23.5	< 0.5	Negative	Negative	6	Viral illness		
62	monica	11	Female	4	11300	56.4	6373.2	34.2	< 0.5	Negative	Negative	4	Viral illness		
63	pavan raj	5	Male	4	9800	67.3	6595.4	13.7	< 0.5	Negative	Negative	3	Viral illness		
64	yogesh	11	Male	3	7600	54.2	4119.2	23.3	< 0.5	Negative	Negative	4	Viral illness		
65	tharish	4	Male	5	9800	63.2	6193.6	45.3	0.5-2.0	Negative	Positive	5	Bacterial illness		
66	naresh	7	Male	2	9800	56.4	5527.2	22.1	< 0.5	Negative	Negative	3	Viral illness		
67	sheebha subhashini	10	Female	5	10200	34.3	3498.6	18.9	< 0.5	Negative	Negative	2	Viral illness		
68	rohini	12	Female	3	14300	72.1	10310.3	23.1	0.5-2.0	Positive	Negative	5	Bacterial illness		
69	keerthana	11	Female	6	6700	45.3	3035.1	10	< 0.5	Negative	Negative	1	Viral illness		
70	chinthana	4	Female	3	9800	54.3	5321.4	10	< 0.5	Negative	Negative	4	Viral illness		
71	nithish	1	Male	2	4500	42.3	1903.5	10	< 0.5	Negative	Negative	4	Viral illness		
72	vignesh	10	Male	4	8900	59.3	5277.7	10	< 0.5	Negative	Negative	3	Viral illness		
73	mukesh	5	Male	1	3900	52.2	2035.8	2.1	0.5-2.0	Negative	Negative	3	Viral illness		
74	santhosh	2	Male	3	9900	57.3	5672.7	1.5	< 0.5	Negative	Negative	3	Viral illness		
75	yashwanth	2	Male	4	6700	67.6	4529.2	23.2	2.1-10	Positive	Negative	5	Bacterial illness		
76	rohini	12	Female	3	9800	34.4	3371.2	27.1	< 0.5	Negative	Negative	5	Viral illness		
77	tharun	6	Male	4	8900	67.2	5980.8	17.1	< 0.5	Negative	Negative	3	Viral illness		
78	lokesh	12	Male	5	10800	23.2	2505.6	9.9	< 0.5	Negative	Negative	4	Viral illness		
79	sivaprakash	2	Male	3	8900	56.4	5019.6	8.9	< 0.5	Negative	Negative	3	Viral illness		
80	sadhana	1	Female	4	7800	23.2	1809.6	43.3	< 0.5	Negative	Negative	4	Viral illness		

81	adhi sankaran	3	Male	2	13400	67.4	9031.6	67.4	0.5-2.0	Negative	Negative	5	Bacterial illness		
82	vetrivel murugan	10	Male	5	8900	56.4	5019.6	23.2	0.5-2.0	Positive	Negative	5	Bacterial illness		
83	sanjai	3	Male	3	9800	72.2	7075.6	12.2	< 0.5	Negative	Negative	4	Viral illness		
84	sabari	3	Male	2	6700	16.2	1085.4	34.2	< 0.5	Negative	Negative	3	Viral illness		
85	harish	12	Male	4	7600	65.4	4970.4	12.3	< 0.5	Negative	Negative	4	Viral illness		
86	adhi sankaran	3	Male	3	12700	76.4	9702.8	32.2	< 0.5	Negative	Positive	4	Bacterial illness		
87	abhinaya	1	Female	1	9700	45.3	4394.1	15.3	< 0.5	Negative	Negative	5	Viral illness		
88	rakesh	10	Male	1	9800	34.3	3361.4	30.2	< 0.5	Negative	Negative	4	Viral illness		
89	dhaswanth	1	Male	2	7800	23.2	1809.6	34.2	< 0.5	Negative	Negative	4	Viral illness		
90	dharshini	4	Female	14	10200	13.5	1377	13.2	< 0.5	Negative	Negative	3	Viral illness		
91	kameshwaran	10	Male	3	6700	35.2	2358.4	23.2	< 0.5	Negative	Negative	2	Viral illness		
92	monica	4	Female	5	8700	34.2	2975.4	13.2	< 0.5	Negative	Negative	5	Viral illness		
93	tamil selvi	4	Female	4	10400	34.1	3546.4	24	< 0.5	Negative	Negative	6	Viral illness		
94	ligiv	12	Female	10	4000	41.5	1660	1	< 0.5	Negative	Negative	2	Viral illness		
95	gokulnath	2	Male	2	11800	76.3	9003.4	45.6	2.1-10	Negative	Negative	2	Viral illness		
96	sangeetha	1	Female	3	8200	60	4920	10	< 0.5	Negative	Negative	3	Viral illness		
97	sivasakthi	5	Male	10	7900	33	2607	25.9	< 0.5	Negative	Negative	3	Viral illness		
98	swetha	5	Female	6	6100	77	4697	1.5	< 0.5	Negative	Negative	3	Viral illness		
99	nancy leena	1	Female	2	15600	91	14196	22.1	0.5-2.0	Negative	Negative	2	Viral illness		
100	kavitha	11	Female	2	6600	51.3	3385.8	4	< 0.5	Negative	Negative	2	Viral illness		
101	bhuvaneswaran	11	Male	2	9100	33.9	3084.9	0.5	< 0.5	Negative	Negative	2	Viral illness		
102	deepak shiva	7	Male	2	10400	78.6	8174.4	16.6	0.5-2.0	Negative	Negative	7	Bacterial illness		
103	jayanthi	12	Female	7	4000	43.6	1744	14.5	< 0.5	Positive	Negative	7	Bacterial illness		
104	santhosh kumar	10	Male	4	4700	68.6	3224.2	2.5	< 0.5	Negative	Negative	3	Viral illness		
105	sutheeshwaran	2	Male	7	3500	35.2	1232	2.2	< 0.5	Negative	Negative	3	Viral illness		
106	sakthivel	1	Male	4	10200	15.9	1621.8	8.9	0.5-2.0	Negative	Positive	4	Bacterial illness		
107	pradeep	3	Male	4	13000	66.4	8632	45.6	0.5-2.0	Negative	Negative	2	Bacterial illness		

108	srilekha	1	Female	7	13000	30	3900	18.8	< 0.5	Negative	Negative	2	Viral illness		
109	bharath	3	Male	3	7100	73.4	5211.4	2.2	0.5-2.0	Negative	Negative	2	Viral illness		
110	pooja	4	Female	30	20100	59	11859	2.1	< 0.5	Negative	Negative	3	Viral illness		
111	dhanya shri	2	Female	14	8200	28.1	2304.2	0.7	< 0.5	Negative	Negative	3	Viral illness		
112	sanjay	7	Male	2	7200	48.2	3470.4	4.5	< 0.5	Negative	Negative	2	Viral illness		
113	kesav kumar	6	Male	7	11400	57.6	6566.4	20.6	0.5-2.0	Negative	Negative	4	Viral illness		
114	narmadha devi	11	Female	7	4000	45.1	1804	2.7	< 0.5	Negative	Negative	6	Bacterial illness		
115	adithiya	8	Male	11	12000	32.8	3936	0.5	< 0.5	Negative	Negative	3	Viral illness		
116	jayaram	3	Male	3	12000	43.2	5184	39.1	0.5-2.0	Negative	Positive	5	Bacterial illness		
117	hariharan	8	Male	4	27000	58.8	15876	155.5	0.5-2.0	Negative	Negative	2	Bacterial illness		
118	sharmila	7	Female	10	20600	76.7	15800.2	36.3	0.5-2.0	Negative	Negative	3	Viral illness		
119	sankar	4	Male	5	4000	50.2	2008	1.6	< 0.5	Negative	Negative	2	Viral illness		
120	yogeshwaran	1	Male	2	6900	43.5	3001.5	21.3	< 0.5	Negative	Negative	2	Viral illness		
121	yogesh	2	Male	3	8200	51.9	4255.8	1.4	< 0.5	Negative	Negative	3	Viral illness		
122	maria yashini	2	Female	2	10100	60.8	6140.8	6.3	0.5-2.0	Negative	Negative	4	Viral illness		
123	gayathiri devi	4	Female	3	12000	61.2	7344	9.3	< 0.5	Negative	Negative	3	Viral illness		
124	jagan	1	Male	2	12800	57.8	7398.4	36.2	0.5-2.0	Negative	Negative	2	Viral illness		
125	srikanth	7	Male	2	9700	57.6	5587.2	13.2	0.5-2.0	Negative	Negative	2	Viral illness		
126	parameshkumar	1	Male	5	15400	54	8316	78.1	0.5-2.0	Negative	Negative	4	Viral illness		
127	gracy	1	Female	5	13800	78.8	10874.4	13.8	< 0.5	Negative	Negative	3	Bacterial illness		
128	dinesh	4	Male	5	12000	64.8	7776	0.8	< 0.5	Negative	Negative	4	Viral illness		
129	jaikishore	4	Male	7	12800	42.4	5427.2	2	< 0.5	Negative	Negative	2	Viral illness		
130	tamil	12	Male	4	8200	60	4920	0.8	< 0.5	Negative	Negative	5	Viral illness		
131	tamilselvi	4	Female	2	12500	82.2	10275	4.9	< 0.5	Negative	Negative	2	Viral illness		
132	kamesh ananthan	1	Male	2	7300	42.7	3117.1	24.4	< 0.5	Negative	Negative	3	Viral illness		
133	ameena yasmin	3	Female	5	6800	21.7	1475.6	1.4	< 0.5	Negative	Negative	3	Viral illness		
134	dharun	2	Male	2	16700	5	835	27.6	< 0.5	Negative	Negative	5	Viral illness		
135	prassana	4	Male	3	9300	64.3	5979.9	26	0.5-2.0	Negative	Negative	5	Viral illness		

136	nithiya	8	Female	7	9000	42.1	3789	31.2	< 0.5	Negative	Negative	2	Viral illness		
137	kamesh suresh	8	Male	3	3600	36.1	1299.6	5.1	0.5-2.0	Negative	Negative	3	Bacterial illness		
138	monish	4	Male	4	12200	83.3	10162.6	1.4	0.5-2.0	Negative	Negative	2	Viral illness		
139	dhanshika	2	Female	5	11200	63.3	7089.6	125	< 0.5	Negative	Negative	3	Viral illness		
140	kaviraj	2	Male	7	9600	35.7	3427.2	11.5	0.5-2.0	Negative	Negative	3	Viral illness		
141	suriya varman	11	Male	3	7300	40.5	2956.5	10	< 0.5	Negative	Negative	3	Viral illness		
142	pramila	5	Female	3	11800	85.2	10053.6	63.3	0.5-2.0	Negative	Negative	3	Bacterial illness		
143	siddarthan	3	Male	4	10200	41.2	4202.4	18.3	< 0.5	Negative	Negative	4	Viral illness		
144	sughasini	4	Female	4	9800	48.9	4792.2	0.5	< 0.5	Negative	Negative	3	Viral illness		
145	hemanth	11	Female	6	11000	67.7	7447	45.6	0.5-2.0	Negative	Negative	2	Bacterial illness		
146	akash	4	Male	7	7900	63.4	5008.6	12	0.5-2.0	Negative	Negative	4	Bacterial illness		
148	abinesh	3	Male	7	11600	37.4	4338.4	35.2	2.1-10	Positive	Negative	5	Bacterial illness		
147	dhanush kumar	4	Male	14	15200	33	5016	10	< 0.5	Negative	Negative	4	Viral illness		
149	vishnal	7	Male	7	5200	52.3	2719.6	86.2	< 0.5	Negative	Negative	5	Viral illness		
150	jenifer	8	Female	4	14000	38.3	5362	10	< 0.5	Negative	Negative	3	Viral illness		
151	yuvaraj	9	Male	3	5900	47	2773	14.7	< 0.5	Positive	Negative	4	Bacterial illness		
152	abishek	3	Male	10	13400	27.4	3671.6	19.5	0.5-2.0	Negative	Negative	10	Viral illness		
153	giridharan	4	Male	20	9300	43.2	4017.6	10.5	< 0.5	Negative	Negative	2	Viral illness		
154	kamalesh	6	Male	10	8900	43.2	3844.8	24.1	< 0.5	Negative	Negative	5	Viral illness		
155	sasvitha sri	6	Female	10	12200	15	1830	26	< 0.5	Negative	Negative	5	Viral illness		
156	rituvarshini	2	Female	4	7900	45.3	3578.7	10.2	< 0.5	Negative	Negative	5	Viral illness		
157	aathira	3	Female	3	13200	63.2	8342.4	34.2	0.5-2.0	Negative	Positive	6	Bacterial illness		
158	megala	5	Female	2	6500	65.3	4244.5	6.3	< 0.5	Negative	Negative	2	Viral illness		
159	vijayranjan	4	Male	4	5600	34.2	1915.2	12.2	< 0.5	Negative	Negative	4	Viral illness		
160	mirthula	1	Female	3	13200	54.3	7167.6	8.9	< 0.5	Negative	Negative	3	Viral illness		
161	rohith	5	Male	4	12000	56.3	6756	12.2	< 0.5	Negative	Negative	3	Viral illness		
162	yaswanth	12	Male	2	8700	34.3	2984.1	6.4	< 0.5	Negative	Negative	2	Viral illness		

163	subiksha	1	Female	3	4500	67	3015	18.3	< 0.5	Negative	Negative	1	Viral illness		
164	eshwanth	5	Male	3	75000	52	39000	12.4	< 0.5	Negative	Negative	4	Viral illness		
165	nithish	1	Male	2	6700	47.4	3175.8	9	< 0.5	Negative	Negative	2	Viral illness		
166	sandhya	8	Female	5	8600	34.2	2941.2	7.9	< 0.5	Negative	Negative	3	Viral illness		
167	karthika	6	Female	4	12900	23.2	2992.8	12.2	0.5-2.0	Negative	Negative	4	Viral illness		
168	monica poongodi	1	Female	3	9200	65.4	6016.8	10	< 0.5	Negative	Negative	4	Viral illness		
169	roopashree	5	Female	5	15300	78.2	11964.6	12.2	0.5-2.0	Negative	Positive	6	Bacterial illness		
170	archana	10	Female	2	16200	77.2	12506.4	45.3	0.5-2.0	Positive	Negative	5	Bacterial illness		
171	hussaini m	7	Female	4	6700	40.6	2720.2	23.2	< 0.5	Negative	Negative	4	Viral illness		
172	hariharan	5	Male	3	7600	23.3	1770.8	14.4	< 0.5	Negative	Negative	1	Viral illness		
173	samiksha	1	Female	1	9800	56.3	5517.4	16.3	< 0.5	Negative	Negative	3	Viral illness		
174	rohith	6	Male	4	10500	62.2	6531	13.4	< 0.5	Negative	Negative	2	Viral illness		
175	sree devi	7	Female	4	8300	23.4	1942.2	9.6	< 0.5	Negative	Negative	4	Viral illness		
176	rithish	5	Male	4	6900	35.3	2435.7	8.4	< 0.5	Negative	Negative	3	Viral illness		
177	alan vino	8	Male	3	7600	34.4	2614.4	11.4	< 0.5	Negative	Negative	3	Viral illness		
178	hemapriya	2	Male	5	6800	45.3	3080.4	19	< 0.5	Negative	Negative	4	Viral illness		
179	naveen	3	Male	1	21000	83.2	17472	56.3	0.5-2.0	Positive	Negative	9	Bacterial illness		
180	saravanan	2	Male	2	9800	43.2	4233.6	12.2	< 0.5	Negative	Negative	3	Viral illness		
181	gomathi	8	Female	3	12400	58.9	7303.6	9.9	< 0.5	Positive	Negative	6	Bacterial illness		
182	akshay	2	Male	2	5900	67.4	3976.6	8.9	< 0.5	Negative	Negative	3	Viral illness		
183	karthikeyan	7	Male	4	14300	61.1	8737.3	12.1	< 0.5	Positive	Negative	4	Bacterial illness		
184	ashwin kumar	4	Male	3	4800	58.3	2798.4	15	< 0.5	Positive	Negative	5	Bacterial illness		
185	akshyashree	1	Female	4	6400	64.8	4147.2	13.5	< 0.5	Negative	Negative	3	Viral illness		
186	roseline	8	Female	4	6100	75.5	4605.5	23.6	< 0.5	Positive	Negative	3	Bacterial illness		
187	vidhyashri	4	Female	3	8500	43.5	3697.5	19.7	< 0.5	Negative	Negative	3	Viral illness		
188	dhanusy	10	Male	2	5900	78.9	4655.1	34.3	0.5-2.0	Negative	Negative	3	Viral illness		
189	dhanushya	10	Female	2	10200	56.3	5742.6	29.8	0.5-2.0	Negative	Negative	3	Viral illness		

190	vignesh	11	Male	3	7400	62.1	4595.4	10	0.5-2.0	Positive	Negative	4	Bacterial illness		
191	john abraham	5	Male	4	8700	45.4	3949.8	10	< 0.5	Negative	Negative	4	Viral illness		
192	sharmila	5	Female	3	12400	56.3	6981.2	10	< 0.5	Negative	Negative	3	Viral illness		
193	manoj	6	Male	2	6400	49.3	3155.2	10	< 0.5	Negative	Negative	4	Viral illness		
194	tanush	2	Male	1	9800	52.1	5105.8	10	< 0.5	Negative	Negative	3	Viral illness		
195	velan	8	Male	5	7800	44.4	3463.2	10	0.5-2.0	Positive	Negative	5	Bacterial illness		
196	vijaya kumar	10	Male	3	3400	38.3	1302.2	31.1	0.5-2.0	Positive	Negative	4	Bacterial illness		
197	jayashree	6	Female	4	8300	71.2	5909.6	21.2	0.5-2.0	Positive	Negative	4	Bacterial illness		
198	santhosh kumar	5	Male	3	9300	43.3	4026.9	8.4	< 0.5	Negative	Negative	3	Viral illness		
199	jaichandran	2	Male	2	10200	34.2	3488.4	5	< 0.5	Negative	Negative	4	Viral illness		
200	soundarya	9	Female	5	7500	54.4	4080	10.3	< 0.5	Negative	Negative	3	Viral illness		
201	anandh	10	Male	3	15200	85.2	12950.4	121.2	2.1-10	Negative	Negative	3	Viral illness		
202	saraswathy	8	Female	3	18000	79.2	14256	65.3	0.5-2.0	Negative	Negative	4	Viral illness		
203	sudharsan	6	Male	2	5600	48.2	2699.2	12.5	< 0.5	Negative	Negative	5	Viral illness		
204	keerthi rajan	3	Male	2	11400	67.2	7660.8	35.3	< 0.5	Negative	Negative	4	Bacterial illness		
205	divya dharsini	8	Female	3	8400	71.2	5980.8	39.4	< 0.5	Negative	Negative	4	Viral illness		
206	arokiya angel vinisha	4	Female	4	7400	67.3	4980.2	19.2	< 0.5	Negative	Negative	5	Bacterial illness		
207	laleb aria	5	Female	3	5600	45.3	2536.8	8	< 0.5	Negative	Negative	3	Viral illness		
208	kavinisha	4	Female	2	6200	54.8	3397.6	9.4	< 0.5	Negative	Negative	5	Viral illness		
209	karthick	5	Male	3	7300	23	1679	13.5	< 0.5	Negative	Negative	6	Viral illness		
210	baby sunitha	1	Female	1	9800	45.3	4439.4	20.3	< 0.5	Negative	Negative	4	Viral illness		
211	rajesh kumar	4	Male	4	10400	34.3	3567.2	19.4	< 0.5	Negative	Negative	5	Viral illness		
212	suresh raju	2	Male	1	11100	54.3	6027.3	15.3	< 0.5	Negative	Negative	3	Viral illness		
213	ugendran	6	Male	3	6800	23.2	1577.6	9.7	< 0.5	Negative	Negative	5	Viral illness		
214	kanishka	3	Female	2	9300	78.3	7281.9	20.2	0.5-2.0	Negative	Positive	3	Bacterial illness		
215	mohana	4	Female	4	5600	45.3	2536.8	17.2	< 0.5	Negative	Negative	5	Viral illness		
216	eashwar baby	2	Male	3	9500	78.3	7438.5	10.8	< 0.5	Negative	Negative	3	Viral illness		

217	lakshmi sree	10	Female	3	8700	23.2	2018.4	15.3	< 0.5	Negative	Negative	5	Viral illness		
218	ramya	2	Female	4	9400	45.4	4267.6	8.3	< 0.5	Negative	Negative	3	Viral illness		
219	ramakrishnan	7	Male	3	4500	34.3	1543.5	16.5	0.5-2.0	Positive	Negative	5	Bacterial illness		
220	kesavarthini	1	Female	2	7200	54.3	3909.6	5	< 0.5	Negative	Negative	3	Viral illness		
221	shakin	4	Female	9	2100	23.2	487.2	17.3	0.5-2.0	Negative	Negative	3	Viral illness		
222	nikitesh	3	Male	3	4800	40.6	1948.8	15.3	< 0.5	Negative	Negative	5	Viral illness		
223	jeyan	3	Male	2	52000	23.3	12116	22.3	< 0.5	Negative	Negative	3	Viral illness		
224	dulasidharan	9	Male	4	7300	56.3	4109.9	17.4	< 0.5	Negative	Negative	4	Viral illness		
225	sankar	4	Male	3	9800	62.2	6095.6	30.2	< 0.5	Negative	Negative	5	Viral illness		
226	vijayan	7	Male	4	11500	23.4	2691	9.4	0.5-2.0	Negative	Negative	4	Viral illness		
227	tamilarasi	4	Male	3	13200	35.3	4659.6	13.5	< 0.5	Negative	Negative	3	Viral illness		
228	jayaram	10	Male	3	14200	34.4	4884.8	25.3	0.5-2.0	Positive	Negative	5	Bacterial illness		
229	ramesh	3	Male	4	8700	45.3	3941.1	23.2	< 0.5	Negative	Negative	3	Viral illness		
230	ashwini	5	Female	2	6800	58.8	3998.4	34.6	< 0.5	Positive	Negative	6	Bacterial illness		
231	satheeshwaran	4	Male	2	5600	76.7	4295.2	8	< 0.5	Negative	Negative	4	Viral illness		
232	durai raj	8	Male	3	4800	50.2	2409.6	6.5	< 0.5	Negative	Negative	4	Viral illness		
233	sridharan	4	Male	2	4300	43.5	1870.5	5.3	< 0.5	Negative	Negative	3	Viral illness		
234	wilson	6	Male	3	9400	51.9	4878.6	14.3	< 0.5	Negative	Negative	3	Viral illness		
235	nazrudeen	5	Male	2	7800	60.8	4742.4	18.8	< 0.5	Negative	Negative	4	Viral illness		
236	hemaroshini	3	Female	3	8700	44.3	3854.1	7.8	< 0.5	Negative	Negative	5	Viral illness		
237	ramya	4	Female	3	8400	57.8	4855.2	17.3	< 0.5	Negative	Negative	4	Viral illness		
238	saravanan	3	Male	2	7600	57.6	4377.6	22.5	0.5-2.0	Negative	Negative	3	Viral illness		
239	lakshanashree	2	Female	4	5600	54	3024	10.9	< 0.5	Negative	Negative	4	Viral illness		
240	gnanasekaran	5	Male	3	11200	78.8	8825.6	12.4	< 0.5	Negative	Negative	3	Viral illness		
241	shakin	4	Female	4	2700	64.8	1749.6	15.7	2.1-10	Negative	Negative	9	Viral illness		
242	madhumari	5	Male	3	9500	42.4	4028	32.2	2.1-10	Positive	Negative	6	Bacterial illness		
243	praveen	4	Male	3	13200	60	7920	33.2	< 0.5	Negative	Negative	4	Bacterial illness		
244	samuel	4	Male	4	12300	82.2	10110.6	29.9	0.5-2.0	Positive	Negative	5	Bacterial		

													illness		
245	sharik	3	Male	2	10500	42.7	4483.5	6.3	< 0.5	Negative	Negative	4	Viral illness		
246	abinaya	4	Female	2	12400	21.7	2690.8	14.3	< 0.5	Negative	Negative	4	Viral illness		
247	vishal	7	Male	4	9430	5	471.5	22.5	< 0.5	Negative	Negative	4	Viral illness		
248	xena	6	Female	3	8940	64.3	5748.42	34.2	2.1-10	Negative	Negative	3	Viral illness		
249	nivetha	6	Female	3	7890	42.1	3321.69	12.6	< 0.5	Negative	Negative	3	Viral illness		
250	sanjay	3	Male	4	4390	56.3	2471.57	7	< 0.5	Negative	Negative	4	Viral illness		
251	preethika	2	Female	4	10200	54.3	5538.6	33.2	< 0.5	Negative	Negative	3	Viral illness		
252	sathya	5	Female	3	14200	61.2	8690.4	30.2	< 0.5	Negative	Negative	4	Viral illness		
253	gokulakrishnan	8	Male	2	6700	55.5	3718.5	23.4	< 0.5	Negative	Negative	3	Viral illness		
254	malarvanan	5	Male	3	4800	71.2	3417.6	45.6	< 0.5	Negative	Negative	4	Viral illness		
255	siva subha	5	Female	2	6700	61.2	4100.4	7.3	< 0.5	Negative	Negative	3	Viral illness		
256	karthick	11	Male	3	8700	56.2	4889.4	14.5	< 0.5	Negative	Negative	4	Viral illness		
257	stenthiramenon	1	Female	3	9300	39.2	3645.6	12.2	< 0.5	Negative	Negative	4	Viral illness		
258	jonatha leoni	3	Female	4	10200	44.3	4518.6	15.3	0.5-2.0	Negative	Negative	3	Viral illness		